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SOME OBSERVATIONS ON BENIGN ŒSOPHAGEAL STRICTURE.[1]

By ROWAN NICKS, M.S., F.R.C.S., F.R.A.C.S.

As this distressing condition often ends fatally unless relieved, ways of dealing with stricture have been developed which vary in complexity from simple dilatation to elaborate replacement *in situ*. In this paper some of the problems of specific surgical reconstruction are discussed on the basis of experience (Table I). The work represents an evolution in surgical thinking and the quality should be judged with this in mind.

There is general agreement that the precise nature of the obstruction must be ascertained by a barium-swallow X-ray examination and by direct œsophagoscopy, at which latter examination dilatation and biopsy are performed as a routine. In most cases tumour, foreign body and cardiospasm are excluded and the ætiology of the stricture is ascertained.

Most resilient and localized strictures of indeterminate, traumatic and healed inflammatory origin respond to dilatation performed by Jackson bougies under vision via the œsophagoscope, or blindly by means of Plummer-Vinson dilators guided along a previously swallowed strong silk thread, which is pulled taut as the prosthesis passes downwards through the stricture.

In the presence of acid reflux with superficial ulceration, œdema and fibrous scarring, relief by dilatation is temporary. In some cases, reflux, previously controlled by the stricture, becomes obvious once again.

In most cases in which strictures are fibrous and quickly recur after dilatation, excision of the strictured segment and surgical reconstruction of the œsophagus are necessary.

Material.

In this experience (Table I), benign strictures have usually presented as late sequelæ of caustic soda burns and of reflux œsophagitis (a heterogeneous group associated with œsophageal scarring, hiatus hernia and operations necessitating ablation of the cardia), and in a peptic ulcer group, including both adults and children, in which the lining membrane of the gullet is of gastric-type epithelium.

Method.

Until recently, surgical treatment by excision of the stricture and reconstruction of the gullet has been only moderately satisfactory.

Most surgeons make a trial of dilatation when there is no active disease and abandon this if difficulty is encountered, or if there is early recurrence.

[1] Expanded from a paper delivered to the Royal Australasian College of Surgeons in August, 1960, at Adelaide.

If hiatus hernia is the basis of a digestive œsophagitis and if the apparent stricture is not in an irreversible stage, and due partly to inflammatory œdema and spasm, cure can be effected by repair (Allison, 1951).

This operation has not proved of value for well-established strictures, and it is in this group that excision and reconstruction of the gullet by the following methods have been practised. The results are assessed on the basis of personal experience. The methods are (i) partial gastro-œsophago-gastrectomy, œsophago-gastrectomy and pyloroplasty (Table II); (ii) gastric exclusion and œsophago-jejunostomy; (iii) segmental replacement with jejunum and pyloroplasty; (iv) sub-total œsophageal by-pass with a segmental graft of caecum and right colon.

TABLE I.

Ætiology of Œsophageal Stricture in this Series (1948 to March, 1960).

Group.	Ætiology.	Number of Patients.
I	Caustic soda burns	9
II	Peptic ulcer	9 (2 adults 7 children)
III	Reflux œsophagitis:	
	Hiatus hernia	3
	Emesis	1
	Cardioplasty	3
	Local resection	2
	Jejunal loop obstruction	1
	Anastomotic leakage	1
IV	Traumatic	1
V	Indeterminate	3
VI	Operation for atresia	2
	Total	35

Extensive Partial Œsophago-Gastrectomy and Pyloroplasty.

Apart from the excision of the stricture, this operation has been elaborated with two objectives—namely, to diminish the quantity of the excessive and highly acid juice by partial gastrectomy, and at the same time to ensure rapid emptying of the stomach contents into the duodenum, by the division of the pyloric sphincter.

After the operation food and digestive juices do not linger in the stomach to prolong the hormonal gastric secretion and to be subject to reflux from changing intraabdominal pressure. The operation has proved to have three disadvantages—namely, a definite mortality in a particular group of sick, anæmic children with peptic ulcer of the œsophagus, incomplete relief of symptoms and some interference with nutrition. Experience with this operation, performed for a number of strictures resulting from varying diseases at different levels within the chest, is summarized in Table II.

Varying degrees of superficial œsophageal ulceration and moderate œsophagitis have been present after operation in all cases at follow-up œsophagoscopic examination. This has necessitated further operation in three cases (two adults and one child).

Pyloric dilatation and not pyloroplasty was usually practised in the earlier cases and this lessens the accuracy of comparison with other methods.

Gastro-Œsophageal Excision with Restoration of Continuity by the Jejunum.

The operation of œsophago-jejunostomy, in which the top of the updrawn first loop of the jejunum is anastomosed to the œsophagus in the chest, the two limbs being decompressed by low entero-anastomosis near the duodeno-jejunal junction, has not been satisfactory in the one case of this series because of partial obstruction of the duodenal loop in continuity with the blind, excluded stomach, which was made manifest by spasmodic obstruction, recurrent œsophagitis and stricture formation. This was relieved only by partial œsophago-gastrectomy and reconstruction by a single Roux-en-Y œsophago-jejunostomy.

The method of reconstruction by a single jejunal tube was first used by Yudin (1944), and later recommended by Allison (1946). The jejunum is divided just beyond the duodeno-jejunal junction and the distal end mobilized on a vascular mesentery by division of the upper jejunal branches of the superior mesenteric artery in such a way that the intercommunicating arcades connecting both arteries and the veins remain as marginal vessels. The mobilized jejunum on its vascular pedicle is updrawn behind the stomach through an avascular area in the transverse mesocolon and anastomosed with the œsophagus. The divided jejunum (acting as a conduit for the undiluted gastric juice and the duodenal contents excluded from contact with food by suture of the cardia) is anastomosed to the antimesenteric border of the adjacent jejunum.

TABLE II.

Analysis of Results of Treatment of Œsophageal Stricture by Resection in this Series (1948 to 1960).

Operation: Partial gastrectomy, pyloromy, intrathoracic gastro-œsophageal anastomosis.

Disease.	Operation, High Anastomosis.	Complications and Follow-up.	Operation, Low Anastomosis.	Disease.
Results of High and Low Anastomosis.				
Caustic	4			Peptic stricture 7
Post-emetic	1			Ruptured caustic 1
Indeterminate	1	7	12	Indeterminate 1
Following perforation	1			Post-operative reflux 1
	1	Anastomotic leak	0	
	0	Deaths	3	
		Cause of death: Shock	2	
		Cardiac infarction with tamponade	1	
Follow-up of Survivors.				
	2	Hæmatemesis	3	
	Fair	Nutrition	Satisfactory, 6 Fair, 2 Poor, 1	
	1	Re-operation	2	
	Satisfactory, 5 Fair, 2	Assessment	Satisfactory 7 Poor, 2	

This operation has proved moderately satisfactory, but at follow-up there have been complaints of bilious regurgitation, diarrhœa, inability to tolerate large meals and the dumping syndrome.

In our series of four cases, the three survivors have eventually had a satisfactory result, although restenosis following regurgitation in one of these had to be treated by local excision and reanastomosis. Death occurred after perforation in one case, that of a child operated upon for a second time for restenosis following œsophago-gastrectomy for primary peptic stricture.

Sphincter Substitution by Segmental Graft of Jejunum.

Reinhoff (1954) advocated direct transplantation of the jejunal segment into the stomach to prevent these sequelæ, but judgement was reserved after a report by Ravitch (1954) on the recurrence of œsophagitis at the anastomosis. There was general interest in the concept of sphincter replacement at this time.

It was shown by Brain (1953) and Merendino (1955) that an isoperistaltic segment of jejunum, transplanted on its vascular pedicle between the ends of the excised œsophagus and the vagotomized cardia, performed satisfactorily as a sphincter substitute, provided that pyloroplasty was done at the same time. The jejunum

protected with abundant mucous and alkaline secretions, cleared food quickly from the gullet into the stomach by peristalsis and was fully protected against acid regurgitation. Any pressure bulid-up and delay of food in the atonic stomach, which might occur after resection of the œsophageal stricture and vagotomy (the vagus nerves often being incorporated in the stricture area), was minimized by pyloroplasty.

The clinical features of two personal cases treated by this method, the results of which have been excellent, are briefly outlined below.

CASE I.—This was a case of peptic œsophageal stricture. The patient was a male, aged 14 years, a malnourished twin who gave a history of lifelong vomiting and feeding difficulty, commencing shortly after birth and accompanied by hæmatemesis. His mother had difficulty in raising him.

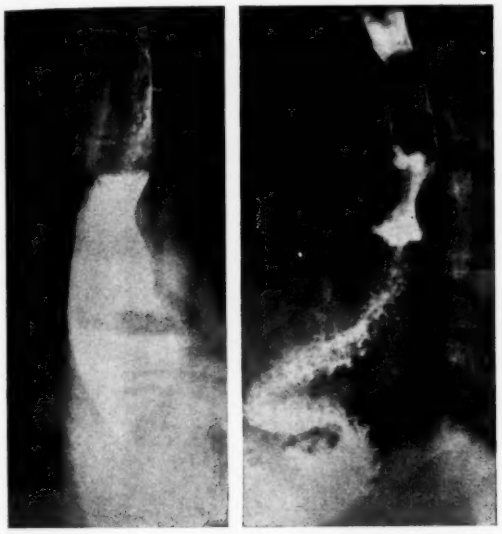

FIGURE I.

Barium-swallow X-ray films of patient described in Case I. *a*: Before treatment; *b*: six months after resection and jejunal graft.

At the time of admission to hospital he complained that he had eaten no solid food for years and that he could swallow milk only. He was desperately thin and miserable. The barium-swallow X-ray examination confirmed the presence of a long stricture in the œsophagus with dilatation above this (Figure I*a*). At œsophagoscopy, a dense stricture with active ulceration was seen in the lower third of the œsophagus. The mucosa was healthy above this. Dysphagia became complete while the patient was waiting for surgery. At operation, which was performed through an abdomino-thoracic incision (Merendino, 1955), the densely adherent and fibrotic œsophageal segment was excised and a segment of jejunum 20 cm. in length was interposed between the upper end of the œsophagus at the level of the inferior pulmonary vein and the cardia of the stomach. A pyloroplasty was performed and the ends of the previously divided jejunum were approximated in continuity. The post-operative course was marred by a high obstruction due to swelling of the jejuno-jejunal anastomosis. This required decompression of the stomach by gastrostomy and entero-anastomosis 14 days later. The patient's present state is excellent. He is active, has gained one and a half stone in weight and takes normal meals without symptoms. There is no reflux. The pre-operative and post-operative barium-swallow X-ray films are shown in Figures I*a* and I*b*. At follow-up œsophagoscopic examination (six months later) there were no secretions in the œsophagus and no œsophagitis at the junction with the normal red jejunal mucosa.

CASE II.—This was a case of peptic œsophageal stricture. The patient was a male, aged 61 years, who complained of progressive dysphagia of three and a half years' duration. A gastro-enterostomy had been performed three years previously. This operation gave no relief and the patient was left with a large abdominal hernia. Before the operation the dysphagia became almost complete. A barium-swallow X-ray examination showed a tight stricture in the lower third of the œsophagus (Figure II*a*), and this was confirmed by œsophagoscopy. He accepted reconstructive surgery gladly, despite his rather unfavourable and surgically complicated general condition. At operation the lower part of the œsophagus was densely adherent and fibrotic. No hiatus hernia was present. Histological section confirmed the presence of columnar epithelium in the ulcerated lumen of the dense stricture. The operation was performed under general anæsthesia in the same manner as previously described, except that care was taken this time to provide a wide anastomotic opening at the divided ends of the jejunum, and since the operation his life has been trans-

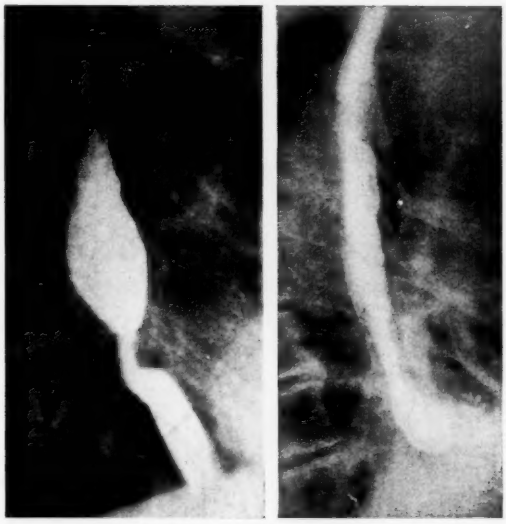

FIGURE II.

Barium-swallow X-ray films of patient described in Case II. *a*: Before treatment; *b*: after resection and insertion of jejunal graft.

formed. He takes all food without restriction or pain, and is robustly healthy. Transient bitterness was experienced from the jejunal juice; this has passed and he is now without symptoms. At œsophagoscopy (June, 1960) there were no secretions in the œsophagus and no inflammation or ulceration of the vividly red jejunal mucosa. The X-ray films of the barium-swallow examination before and after the operation are shown in Figures II*a* and II*b*.

Subtotal Anterior-Mediastinal Extrapleural Œsophageal By-pass Using Colon.

The advantages of this operation are many—namely, that the large bowel has abundant length and an adequate blood supply from the middle colic vessels, and is isoperistaltic, easily sterilizable, resistant to gastric reflux and free from the discomfort of the dumping syndrome.

The upper end (the caecum) is passed behind the sternum and anastomosed with the upper end of the divided œsophagus in the neck. The pleura is not opened. In the event of leakage, this occurs safely in the neck.

Little shock occurs, despite the magnitude of the procedure and, should it be necessary to remove a carcinoma, this can be done very completely at a short, second-stage operation without danger of perforation.

Personal experience is limited to one case of benign stricture which will be described, and three cases of carcinoma. The course was remarkably free from shock and post-operative complications in all, apart from a temporary cervical fistula in a man, aged 79 years, with

an inoperable carcinoma of the lower part of the œsophagus.

CASE III.—This was a case of an extensive caustic-soda stricture. The patient was a female, aged 43 years, who was admitted to hospital complaining of severe and progressive dysphagia, which had become impossible to manage by œsophageal dilatation. At two years of age, after the patient had swallowed caustic soda, gastrostomy was performed for feeding purposes and the œsophagus was kept open by retrograde dilatation until she reached the age of 35 years, when the gastrostomy was allowed to close. In the meantime she had married and had two children, but had never taken solid food.

For the past eight years the stricture had been dilated at decreasing intervals, but this procedure had recently become difficult and required repetition at monthly intervals. The barium-swallow X-ray examination (Figure III*a*) demonstrated a tight stricture at the aortic arch, which was confirmed at œsophagoscopy. The œsophageal mucosa was healthy above the stricture. A by-pass was planned, in which the colon would be used in preference to the jejunum, because of the high level of the stricture. The bowel was prepared for four days prior to the operation, by daily washouts and neomycin by mouth. Through a cervical incision with an extension downwards dividing the sternum into the second intercostal space on either side, the cervical and upper thoracic part of the œsophagus was isolated and divided, the trachea and left recurrent laryngeal nerve being pulled to one side. The lower end of the œsophagus above the stricture was carefully inverted. By means of a long mid-line abdominal incision, the caecum and ascending colon, together with the mesocolon, were mobilized from the posterior abdominal wall, and the ileo-caecal artery was divided at its origin. The ileum was divided just proximal to the ileocaecal valve, and each end was closed and inverted. Appendicectomy was performed. It was found that adequate length of colon was made available by the use of a pedicle containing the right colic artery. The colon was divided proximal to the middle colic vessels.

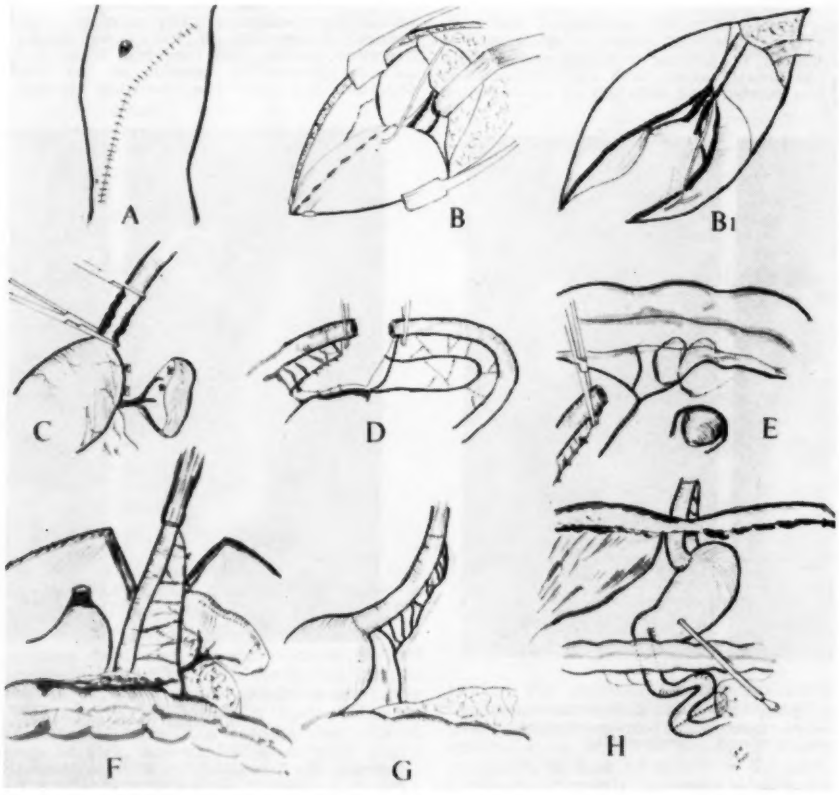

FIGURE III.

Steps of jejunal grafting. (Cases I and II.) *a*: Abdomino-thoracic incision; *b*, *b*1: incision of diaphragm made to avoid phrenic nerve; *c*: excision of œsophageal stricture; *d*: preparation of jejunal pedicle; *e*: passage of jejunal pedicle through the mesocolon; *f*: suture of this to upper end of intrathoracic portion of œsophagus; *g*: suture of divided lower end to cardia; *h*: segment in place, diaphragm sutured, bowel reconstituted, pyloroplasty performed and gastrostomy tube in position.

Continuity of the bowel was restored by an ileo-transverse colostomy. The caecum and ascending colon were withdrawn through a tunnel between the diaphragm and sternum and delivered into the neck, where an anastomosis was made with the upper end of the divided œsophagus. The lower end of the colonic segment was anastomosed to the anterior surface of the lesser curvature of the stomach. The operation was completed by two necessary procedures—namely, pyloroplasty, to prevent stasis in the stomach, and gastrostomy, to guard against ileus. An X-ray film taken on the portable machine after operation showed no pneumothorax. The patient's post-operative convalescence was uneventful. At follow-up four months after operation she had gained three stone in weight, had no regurgitation and swallowed all food without discomfort. The barium-swallow X-ray examination (Figure III*b*) shows no delay in the œsophagus and normal colonic haustrations of the colon in the anterior part of the mediastinum. There was no reflux into the colon, but some occurred into the scarred lower inverted part of the œsophagus extending from the cardia.

Results.

The overall follow-up results in a series of 35 cases of benign stricture treated by various techniques is shown graphically in Table III.

Discussion.

It is clear that the progression of œsophagitis to ulceration, with hæmorrhage, spasm, and finally, stricture formation, is due in most cases to swamping and active digestion of the largely unprotected squamous œsophageal epithelium, or abnormal columnar epithelium lining the gullet, by potent gastric juices.

The strictures may be acquired from reflux (Allison, 1946), from vomiting (Quinke, 1879) or from scarring as a result of burns, trauma and ulcer (Tileson, 1906), and from surgical operations necessitating ablation of the cardiac sphincter, such as cardioplasty and intrathoracic œsophago-gastrostomy. If the stomach is dislocated into the chest, the pinchcock action of the diaphragmatic hiatus, acting as a confining girdle about its waist, augments the swamping of the mucosa with digestive secretions during changes in intraabdominal pressure.

As a general principle for the treatment of œsophagitis resulting from misplacement, an attempt is made to

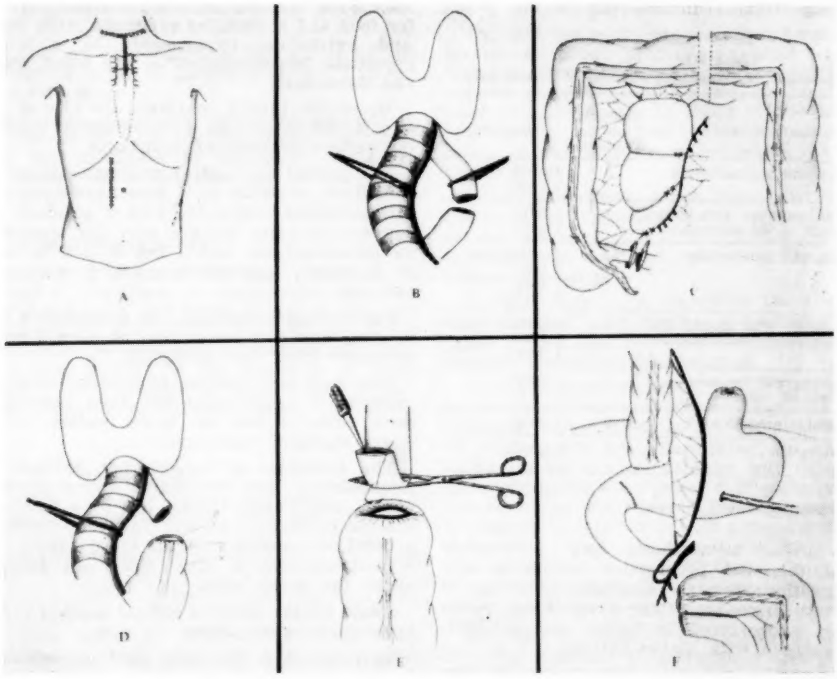

FIGURE IV.

Steps in the right colon by-pass operation performed in Case III. *a*: Cervico-sternal-abdominal incision; *b*: isolation of cervical portion of œsophagus with division and closure of the lower end; *c*: preparation of the right colon with ligature of the right colic and ileo-colic vessels; *d*: caecum delivered into neck (the appendix having been removed and the terminal ileum closed); *e*: œsophago-caecal anastomosis; *f*: completed operation showing vascular pedicle to the colonic œsophagus, the lower gastro-colic anastomosis and the reconstruction of the bowel by a lateral ileo-colic anastomosis. The outflow from the stomach has been safeguarded by pyloroplasty and a gastrostomy tube.

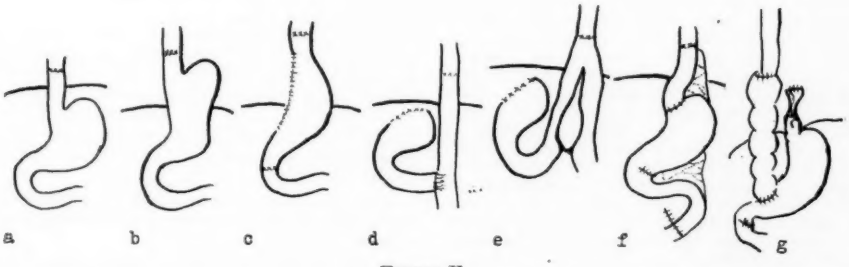

FIGURE V.

Various operations for œsophageal stricture (see Table III). *a*: local excision or plastic reconstruction; *b*: local excision and vagotomy with intrathoracic dislocation of the stomach; *c*: partial gastrectomy and pyloroplasty; *d*: partial œsophagectomy with gastric exclusion and Roux-en-Y reconstruction with jejunum; *e*: partial œsophagectomy with ileo-œsophagostomy and entero-anastomosis; *f*: excision and jejunal interposition; *g*: colonic by-pass operation.

confine the stomach below the diaphragm, either by posture or by surgical replacement (Allison, 1946).

The progression of reflux ulceration from hiatus hernia, despite conservative medical measures, can be arrested and cured by surgical restoration only (Allison, 1951).

An abnormal lining of the gullet, whether of true gastric epithelium containing peptic and oxyntic cells (Barrett, 1954), or of partially differentiated columnar epithelium, frequently undergoes grave pathological changes at any age. These include penetrating peptic ulceration with pain, hæmorrhage and perforation (especially in adults), and progressive ascending œsophageal fibrosis with extensive ulceration leading to marasmus and death from inanition—a condition which is more commonly encountered in babies and children, and used to be confused with hiatus hernia.

TABLE III.[1]
Results of Various Operations for Œsophageal Stricture in Present Series.

Operation.	Number of Patients.	Results.
I. Local excision or plastic reconstruction	6	4 good. 2 poor.[2]
II. Local excision and vagotomy with intrathoracic dislocation of the stomach.	2	1 fair. 1 poor.
III. Partial gastrectomy and pyloroplasty ..	19	12 satisfactory. 2 fair. 2 poor. 3 deaths.
IV. Partial œsophagectomy with gastric exclusion and Rous-en-Y reconstruction with jejunum.	4	2 good. 1 fair. 1 death.
V. Partial œsophagectomy with ileo-œsophagostomy and entero-anastomosis.	1	1 poor.
VI. Excision and jejunal interposition ..	2	2 good.
VII. Colonic by-pass operation	1	1 good.

[1] See also Figure V.
[2] Poor results in peptic stricture.

CASE IV.—The patient was a male, aged five years, who was admitted to hospital in 1953 with a history of vomiting since birth. At this examination spasm and ulceration of the lower part of the œsophagus were present. A diagnosis of reflux ulceration from hiatus hernia was made and repair was carried out. No relief followed from the vomiting or the hæmatemesis. Radiologically there was no evidence of recurrent hiatus hernia. Resection was carried out in 1954, a year after the first abortive operation. At thoracotomy there was severe periœsophagitis and thickening of the lower segment of the œsophagus. An extensive upper gastro-œsophageal resection, combined with pyloroplasty, was performed. A large peptic ulcer was found penetrating the antero-medial wall of the œsophagus just above the hiatus. The greater curvature of the stomach was fashioned into a tube, at the upper end of which a gastro-œsophagostomy was performed, and this anastomosis was ineverted in an attempt to make a valvular entrance. Convalescence was uneventful. The pathologist reported that the specimen he was given was a thick, fibrotic segment of œsophagus, with ulceration of the mucosa. There was a deep ulcer crater in the antero-medial wall measuring 1·5 cm. in diameter. The lining of the mucosa was of an abnormal gastric type containing oxyntic cells. At follow-up examination in April, 1960, the patient was reasonably well, but had occasional dysphagia.

Most surgeons have been content with partial gastrectomy and intrathoracic gastro-œsophagostomy (Sweet, 1946) supplemented more recently by a pyloroplasty to drain and decompress the atonic vagotomized stomach. Belsey (1953) reported good results with this technique and the long-term follow-up results in the present series have been moderately satisfactory. Cooley (1954) reported that the stomach drained well, and that reflux was not a problem after high intrathoracic gastro-œsophageal anastomosis. He advocated this operation with pyloroplasty for all cases of œsophagectomy irrespective of the pathological lesion, and certainly the high anastomosis has been more satisfactory in our own series (Table II).

Allison (1946), aware of the probability of digestive œsophageal restenosis, advocated, at this time, exclusion of the stomach from swallowing and reconstruction of the gullet with a jejunal segment (Yudin, 1944).

There has not been general satisfaction with this operation. Some patients develop reflux of bile and gastric juice with stenosis, and some complain of a small capacity for food and a dumping syndrome with diarrhœa, flushing and nutritional impairment. In a few cases peptic ulceration has developed in the blind, excluded stomach and duodenum.

Merendino (1955), conceived the idea of using a segment of jejunum to provide a physiological sphincter to replace the excised segment of œsophagus.

The jejunal segment approximates to an ideal sphincter substitute, allowing as it does reconstruction of the gullet in anatomical continuity with a segment of bowel which delivers contents quickly into the stomach (apart from an occasional air lock), but is not in itself susceptible to digestion, provided there is a wide outlet from the stomach.

Our limited experience has confirmed a gratifying relief of symptoms and restoration of normal eating habits and nutrition after this operation.

The case for surgical techniques employable for total œsophageal replacement has been hammered out at the same time as that for more limited, but problematical, lesser segment replacements.

The technique of retrosternal, intracervical œsophago-jejunostomy, first introduced independently by Rienhof (1943) and Yudin (1944), has been developed with some success by Robertson and Sarjeant (1950), but with the general reservation that the blood supply of the displaced jejunal segment is often uncertain for an anastomosis above the aortic arch.

Sweet (1946) restored several cases of very high stricture by œsophago-gastrostomy.

This technique has been used successfully in two cases in our own series, but it is a long dislocation of the bulky stomach which may restrict lung function.

It has been supplanted by segmental grafting of the small bowel, or preferably a segment of the large bowel, which has an excellent blood supply, a loose mesentary, is free from the dumping syndrome can now be sterilized.

The left half of the colon was successfully used for total œsophageal replacement after excision of a tumour in the pharynx by Golligher and Robin (1954), who quoted earlier work by Egidi, the Italian surgeon, who successfully used the transverse colon, and the French surgeons Orsini and Toupet (1950) and Rudler (1951), who used both the right and the left halves of the colon for a segmental by-pass for both benign stricture and carcinoma. At this time Rudler reported 28 cases; in 13, leakages occurred at the upper end and the patients died. Since this time methods for bowel sterilization have been refined, and neomycin is available for the purpose (Neville and Clowes, 1958).

This procedure allows excellent palliation for inoperable carcinoma of the œsophagus, and almost total resection for operable cases.

In one interesting case in my experience, a total replacement of the œsophagus was accomplished in a female patient, aged 71 years, who had a slowly growing carcinoma of the cervical part of the œsophagus and hypopharynx, by the ascending colon and the caecum. The convalescence was uncomplicated (apart from a little difficulty she had for a week or two) in getting used to swallowing without inhalation into the trachea. Reconstruction was possible without the mutilation of a laryngectomy, which had to be performed in Golligher's case. Palliation has been excellent until now, eight months later, when there is widespread recurrence in the cervical glands.

Summary.

Some of the problems encountered over a twelve-year period in a series of 35 cases of benign œsophageal stricture have been discussed.

The problem of benign peptic stricture in adults and children is reviewed in more detail. Two cases, in which the stricture has been excised and sphincter substitution made by means of a segment of jejunum interposed in continuity between the œsophagus and the cardia, are presented.

The total replacement or by-pass of the gullet by the caecum and ascending colon is discussed in the light of a small personal experience.

The follow-up results of excision, œsophago-gastrostomy and œsophago-jejunostomy used to reconstruct the intrathoracic part of the œsophagus in this small series are presented and compared with those of recent bowel replacements *in situ*.

Acknowledgements.

Some of the cases were performed at the Thoracic Unit, Green Lane Hospital, Auckland, in conjunction with Sir Douglas Robb, F.R.C.S., and Mr. David Cole, F.R.C.S., and with Mr. A. F. Grant, F.R.C.S., at the Royal Prince Alfred Hospital. Their work is gratefully acknowledged. Mr. David Cole was most helpful in the follow-up of cases from Green Lane. The photographs were taken by Mr. Woodward-Smith, Department of Illustration, University of Sydney.

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AN INVESTIGATION INTO THE INCIDENCE OF REACTIONS FOLLOWING THE INJECTION OF TETANUS ANTITOXIN.[1]

Recorder: ANDREW FRASER, M.B., B.S.,
Melbourne.

Object of the Investigation.

THE last few years has seen considerable interest in, and speculation about, protection against tetanus. There has been considerable disagreement about the most desirable method of preliminary testing for serum sensitivity, the most effective course to adopt in providing protection in both unimmunized and immunized individuals and the safety of any such procedure which the practitioner may decide to use.

It was these facts which stimulated the Research Committee of the Victoria Faculty to investigate some aspects of this problem, and it was finally decided to study the incidence of reactions following the administration of tetanus antitoxin.

To our surprise, a search of the literature up to the time that the investigation was commenced in May, 1958, failed to find that any such forward study of this problem had previously been documented.

It was believed also that, in addition to determining the incidence of local and general reactions following tetanus antitoxin administration, the investigation would provide an opportunity of determining to what extent active immunization against tetanus was being carried out in the community after passive tetanus prophylaxis—a procedure which we believed from personal experience was tending to be ignored in both private and hospital practice.

Method.

Two forms for completion by those taking part in the investigation were finally produced.

The first of these forms (Figure I) was to be filled in for each injection of antitetanus serum given. It will be seen that, in addition to the patient's age and sex, information about the test dose given was sought, together with the amount in units, the batch number and the route of administration of the full prophylactic dose. It was this form which recorded whether a reaction had occurred or not, whether active immunization had been started, and, if so, at what interval after the giving of antitoxin. With this form and accompanying instructions for its completion, each participant in the investigation was advised of modern views in the lack of reliability of the so-called skin test and the advice of such workers as Laurent and Parish that the administration of one-tenth of the intended prophylactic dose by the subcutaneous route was a safe and reliable procedure. I have become aware subsequently that such a routine is considered by some to be not as safe as Laurent and Parish affirm; nevertheless, our advice was largely heeded, and as you will learn, no alarming reactions to the initial dose were experienced.

A further form designated "B" was drawn up to be completed for each case in which a reaction occurred. As will be seen (Figure II), it asked for almost a wealth of detail, and we apologize for inflicting such a lengthy document on those of our members who were required to complete it. The clinical observations it required are listed in the form, and people were, in the main, most painstaking in its completion.

These forms, together with instructions for their completion (see appendix) and the advice about skin testing previously mentioned, were forwarded to the 203 members

[1] An investigation undertaken by the Research Committee of the Victoria Faculty of The Australian College of General Practitioners from May, 1958, to October, 1959. This article is based on a paper delivered to the General Practitioners' Convention in October, 1960, in Melbourne.

and associates then constituting the Victoria Faculty. Reports were received from 43 members. The investigation was terminated in October, 1959, the survey thus lasting about 18 months.

Analysis of Results.

Incidence of Reactions.

The material obtained for analysis from the 43 participants provided the following over-all figures. The total number of antitetanus injections given was 2116. The number of reactions recorded following these injections was 156 (7·4%). Of these, general reactions accounted for 95 (4·3%) and local reactions for 61 (3·1%). The number of patients subsequently actively immunized was 784 (37·1%).

FORM "A"

THE COLLEGE OF GENERAL PRACTITIONERS

(Victoria Faculty)

INVESTIGATION INTO THE INCIDENCE OF REACTIONS FOLLOWING THE INJECTION OF TETANUS ANTITOXIN

Name of Doctor _____ Address _____

Case No.	Date	Patient's Initials	Age	Sex	Test Dose		Prophylactic Dose			Reaction (Yes or No)	Was Active Immunisation Commenced (Yes or No)	If so, how long after administration of A.T.S.
					Amount in c.c.	Route given	Amount in units	Batch No.	Route given			

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FIGURE I.
Form "A".

In the 82 delayed reactions analysis provided the clinical features shown in Figure V.

It will be seen that all patients developed an urticarial rash, but the other manifestations of serum sickness occurred comparatively rarely.

There were no cases of radiculitis, even though investigators had been made aware of this rather rare complication of serum reactions in our initial letter to them. Two patients were reported as having severe headache, and in three the reaction was accompanied by abdominal pain and vomiting. There was one case of polyarthritis and one patient developed a petechial rash in addition to urticaria.

Of the patients with local reactions, all cases were reported as developing erythema and induration, but there were no cases of local sloughing, local neuritis or other abnormalities at the local site.

Measures used to deal with reactions both local and general seemed surprisingly limited and the antihistamines held pride of place in treatment.

Clinical Failure of Reactions.

The analysis of the information obtained from the form listing details of the reactions which occurred was the next task.

The question "Had the patient previously had A.T.S.?" provided 84 positive replies, 60 negative and 12 unknown. This provided a figure of 58·4% of patients who had previously had an injection of horse serum.

With regard to the allergic history our figures revealed that 41 (32%) individuals who had a reaction had had a previous allergic episode or episodes. By far the greatest group gave a history of hay fever (20), followed by skin manifestations (14), drug reactions (9), asthma (5) and eczema (3).

Twenty-one (15·2%) of those experiencing a reaction had a positive family history of allergy. This number was made up of sufferers from asthma (12), hay fever (5), eczema (3) and skin and drug reactions (2 each).

Turning now to the clinical features of the reactions which occurred, it can be said at the outset that none was of the serious anaphylactic type and none of the reactions appeared really to worry the observing doctor.

Of the 61 local reactions (Figure III), 41 (67·3%) occurred in less than 24 hours after the giving of antitetanus serum—the majority within several minutes of the injection and 20 (32·7%) later than 24 hours after the injection—the longest interval being seven days.

Of the 95 general reactions, 13 (13·7%) occurred in less than 24 hours and 82 (86·3%) after a period longer than 24 hours, mostly seven to ten days after the giving of antitetanus serum. Our figures did not show any correlation between the personal or family allergic history of the individual and the time interval of the reaction.

The clinical features of the more important immediate general reactions, of which there were 13, are summarized in Figure IV.

Of these 13 patients, three subsequently developed a delayed general reaction in less than 12 hours. Two more developed this type of reaction 36 hours and seven days after the initial reaction—the latter period being the usual time-interval before onset of a delayed reaction.

Treatment of Reactions.

For treatment of the 61 local reactions, adrenaline, given by the subcutaneous route, was favoured in two cases only. Antihistamines were given by the oral route in 13 cases and intramuscularly in four, and the product "Avil" appeared to be the choice of most. The corticosteroids were employed by no one.

A somewhat similar picture was presented in measures used to treat the 95 general reactions. Adrenaline was given on four occasions only—once subcutaneously and three times intramuscularly. Antihistamines were given in 23 cases (in 19 orally and in four parenterally), and once again the corticosteroids were not employed. No patient apparently developed respiratory difficulty severe enough to warrant the administration of oxygen, and tracheotomy certainly was never required.

Ten observers expressed themselves as satisfied with the measures used to alleviate the effects of local reactions and six were similarly pleased with their treatment of general reactions.

Period of Disability.

With regard to the amount of disablement which followed these reactions, our figures showed that amongst the 61 cases of local reactions no invalidism occurred in 41 (67%); two patients were disabled for one day and one patient for two days, and the longest period of disablement was four days.

The degree of disablement in patients experiencing a general reaction was naturally greater. Figure VI summarizes the details of the disablement of the 95 patients who experienced this type of reaction.

Patients who experienced the longer periods of disability were noted particularly to suffer from joint pains.

Incidence of Active Immunization following a dose of Antitetanus Serum.

It will be remembered that those taking part in the investigation were asked to record whether active immunization had been performed after administration of antitetanus serum, and it was interesting to see the varying pattern of procedure which they adopted.

FORM "B" THE COLLEGE OF GENERAL PRACTITIONERS
(Victoria Faculty)

CASE RECORD OF REACTION FOLLOWING INJECTION OF TETANUS ANTITOXIN

NAME OF DOCTOR :

ADDRESS :

CASE No.:

PATIENT'S INITIALS :

DATE :

Please answer "YES", "NO", or "UNKNOWN" where applicable

1. Had patient previously received A.T.S. or other horse serum? (e.g., diphtheria antitoxin or snake antivenene)
2. If so, was there any previous reaction to it?
3. What was the nature of this reaction?
4. What other drugs (e.g., Penicillin), if any, were administered at the same time?
5. Is there any previous history of allergy? Personal : Family :
   e.g., Asthma
   Infantile Eczema
   Hay Fever
   Urticaria
   Hives
   Reactions to any other drugs
6. Clinical features of reactions :
   (A) Interval between injection and onset of reaction :
   Minutes
   Hours
   Days
   (B) In the case of immediate reactions
   a. Can the possibility of intravenous administration be reasonably excluded?
   b. Were the following features present :—
   i. Fall in pulse volume (or B.P.)
   ii. Loss of consciousness
   iii. Rash
   iv. Oedema
   v. Respiratory difficulty :
   Laryngeal obstruction
   Bronchospasm
   Pulmonary Oedema
   Hyperpnoea
   vi. Pyrexia Chill or Rigor
   vii. Other
   c. Was there any subsequent development of a delayed reaction? (see below)
   d. How long did the reaction last?
   e. Did death occur?
   (C) In the case of delayed reaction were the following present :—
   a. General reactions :
   i. Pyrexia
   ii. Urticaria
   iii. Lymphadenopathy
   iv. Splenomegaly
   v. Oedema
   vi. Joint pains
   vii. Radiculitis or neuritis
   viii. Other
   b. Local reaction :
   i. Erythema and induration
   ii. Sloughing
   iii. Local neuritis
   iv. Other
7. Treatment and progress
   a. Therapy—Were the following administered and in what dosage :—
   i. Adrenalin— Subcutaneously / Intramuscularly
   ii. Antihistamines— Oral / Parenteral
   iii. Corticosteroids— Oral / Parenteral
   iv. Oxygen
   v. Was tracheotomy necessary
   vi. Any other drugs or measures
   b. What was your opinion of the efficacy of the measures which you used?
   c. What was the degree of disablement of the patient? (Duration of absence from employment, school, etc.)

Comments :—

FIGURE II.
Form "B".

Some observers obviously did not consider offering active immunization to their patients, and in other cases when it was offered it was noted that the patient refused this permanent protection. In my own experience it is often surprising to find how hard it is for an intelligent patient to grasp the meaning of active immunization against tetanus, even when the analogy of diphtheria immunization is, for example, drawn; but if one's patience is rewarded by the patient's acceptance of tetanus toxoid, the very real worry of the patient's returning with a fresh wound requiring tetanus prophylaxis only a few weeks after a dose of antitetanus serum has been given is avoided.

The time elapsing between the administration of antitetanus serum and the subsequent commencement of active immunization varied a lot, and some observers appeared not to favour any set interval for the procedure to be started.

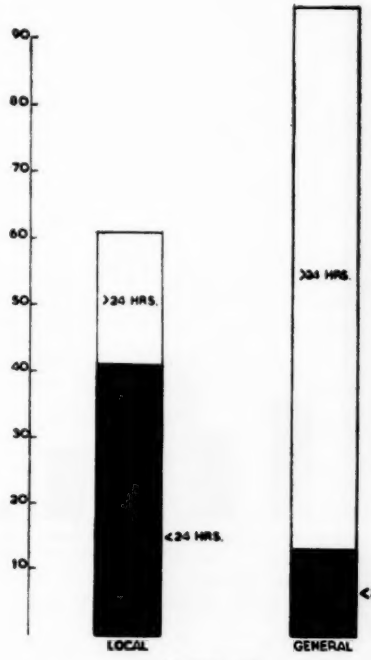

FIGURE III.
Time incidence of reactions.

Differing views are held as to the desirability of giving tetanus toxoid coincidently with antitoxin. There are those who say that, in the presence of circulating anti-

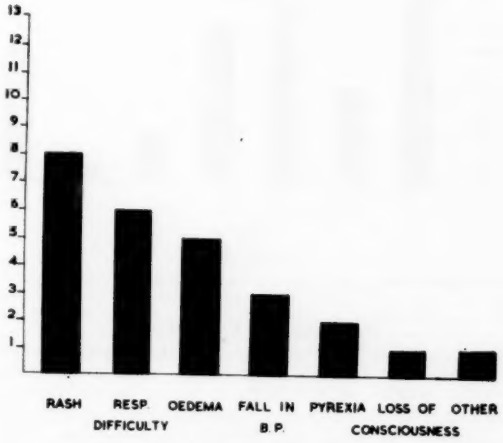

FIGURE IV.
Clinical features of 13 immediate general reactions.

toxin in the system, the antigenic response to toxoid will not be as great as when administration is delayed until passive antitoxin has disappeared from the body in from three to four weeks.

Be that as it may, to 485 (62%) of the 784 patients who received active immunization, tetanus toxoid was given coincidently with antitoxin. To 68 (9%) it was given subsequently, but in the first week; to 85 (12%) in the second week; to 37 (6%) in the third week; to 41 (7%) in the fourth week; and to 27 (4%) after a period of longer than a month (Figure VII).

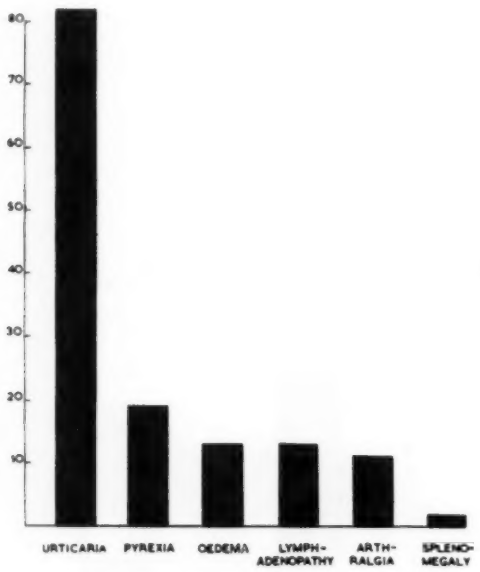

FIGURE V.
Clinical features of 82 delayed general reactions.

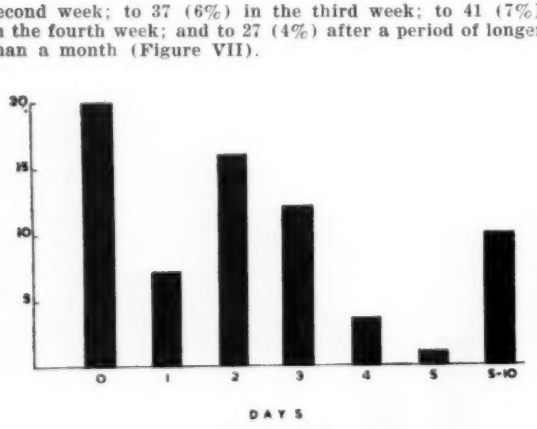

FIGURE VI.
Duration of disablement in 95 general reactions.

Summary and Conclusions.

This completes the analysis of the data which our observers recorded and two main conclusions emerge from the results we obtained.

The first of these is that, after an injection of tetanus antitoxin, a reaction can be expected in some 7% of patients. Of this number the reaction will consist of local swelling and discomfort in 3%, and the more important general reaction of serum sickness in 4%, usually seven to ten days after the injection has been given (Figure III).

The second is that active tetanus prophylaxis is still being accepted by only one-third of patients who have undergone passive serum prophylaxis. This is a disturbing and dangerous fact, and this investigation will have achieved at least something if the performance of active immunization is stimulated amongst general practitioners.

Acknowledgements.

My thanks are due to all those members of The Australian College of General Practitioners who contributed the material for this investigation; I know how hard completing forms such as these can be in a busy surgery session. Particularly grateful am I to my fellow members of the Research Committee, and especially so to Dr. David Pitt, chairman, whose wisdom and experience in research set the investigation on its way, and who gave so much help in the final analysis of the figures.

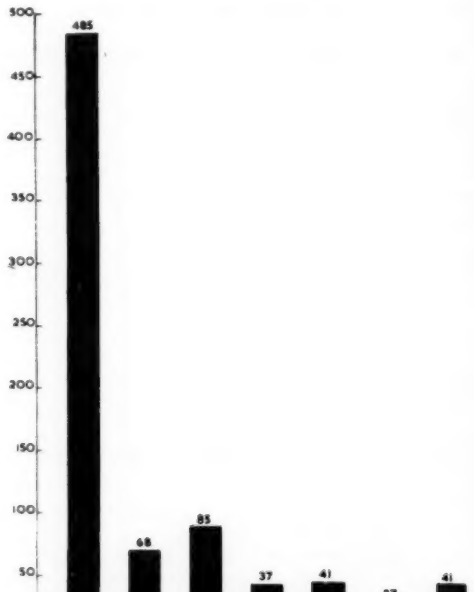

FIGURE VII.
Time interval of active immunization after the administration of anti-tetanus serum in 784 cases.

Appendix.

The following intructions were supplied to observers together with forms "A" and "B".

THE COLLEGE OF GENERAL PRACTITIONERS

(Victoria Faculty)

Notes on the Investigation

The College is endeavouring to determine the incidence and nature of reactions following the administration of tetanus antitoxin. This common procedure and its reactions has received surprisingly little attention in the past, and a recent search of the literature has revealed only one series of forward investigation such as this now planned by the College.

Coincidently information is being sought on whether or not active immunisation is being carried out subsequent to tetanus antitoxin prophylaxis. It is felt that at present, active immunisation is not being performed to the extent that it should.

The completion of the questionnaire at first sight, would appear time-consuming, but it must be remembered that in the majority of cases it will be necessary to complete Form "A" alone and that Form "B" is for use only in those cases reacting to tetanus antitoxin.

Notes on the Questionnaire

FORM "A"

1. "Was active immunisation against tetanus performed or recommended?"

The College is anxious to extend the practice of active immunisation against tetanus and it is suggested that this investigation might be the means of stimulating this aspect of tetanus prophylaxis.

2. "Was a test dose given?"

The attention of participants in this investigation is drawn to the serious doubt which has been cast on the reliability of intradermal testing with horse serum. Positive tests have been followed by intramuscular injection of tetanus antitoxin with impunity, whilst negative tests have been followed by serious or even fatal reactions.

Laurent and Parish, noted workers in this field, suggest that the administration by the subcutaneous route of 0·1 ml. of the dose of A.T.S. to be given; if this is not followed by a general reaction in 30 minutes, it can be followed by administration of the full dose of antitoxin with safety.

FORM "B"

1. "Is there any previous history of allergy?"

Infantile eczema and asthma are of particular significance.

2. "Clinical features of reaction."

Severe anaphylactic reactions always occur a few minutes, up to a maximum of two hours following administration of serum. Serum sickness in an accelerated form in 3-4 days or delayed for 7-12 days.

Since mild reactions of this type are frequently overlooked by the patient or attributed to some other cause, investigators are asked to acquaint patients under observation with these facts.

Local reactions usually occur at the end of the first week after administration.

Neurological complications (radiculitis and neuritis) occur usually 3-4 days after the onset of serum sickness and involve most frequently the brachial plexus area. The radial nerve and optic nerves are occasionally involved, but much less frequently.

3. "Treatment and progress."

Investigators are asked to record the dosage and variety of therapeutic agents used.

Investigators are asked, if possible, to return Form "A" one month after, and Form "B" as soon as possible after completion.

THE RELIABILITY OF METHODS FOR CHOLESTEROL DETERMINATION IN STUDIES ON CORONARY DISEASE.

By W. D. BROWN, B.Sc. (Adelaide), Ph.D. (Birmingham),
National Health and Medical Research Council Senior Research Fellow, Kanematsu Institute, Sydney Hospital.

IN 1949, Steiner pointed out the difficulty in assigning a rôle to hypercholesterolæmia in coronary disease due to the possibility that the highest levels within the wide range of so-called "normal values" for serum cholesterol are atherogenic. In 1958, Schaeffer *et alii* pointed out that the diagnostic value of estimates for serum cholesterol is enhanced when the normal range is defined more precisely by relating the values for serum cholesterol levels to the normal factors known to affect them at the time of their determination. These factors include menstrual cycle and pregnancy and other factors related to sex and heredity, age, diet and emotional stress. It is also evident from the magnitude of the errors found in the determination of serum cholesterol level (Brown, 1961*a*) that technical errors may be as troublesome as any other factor in the location of serum cholesterol levels within the normal range, which is usually regarded as being from 150 to 300 mg. per 100 ml.

It has been pointed out that saponification is a useful step in the accurate determination of serum cholesterol level (Brown, 1961*a*), and in this paper further observations are made on this subject. The accuracy obtained by determination of serum cholesterol after its isolation in the non-saponifiable extract is examined after direct saponification of serum in a manner slightly modified from that introduced by Abell *et alii* (1952). The standard values are obtained after further purification of the cholesterol with digitonin (Brown, 1961*b*). The most influential method of serum cholesterol determination in which saponification is omitted is due to Zlatkis *et alii* (1953), and the errors in this method are examined in detail. The information obtained in the course of the various studies on serum cholesterol determination is used to show the importance for epidemiological studies on coronary disease of improving the accuracy of this determination.

Materials and Methods.

In the method of Zlatkis *et alii* (1953), "Ajax" sulphuric acid AR was used (Brown, 1961*a*) and the acetic acid was purified according to the method of MacIntyre and Ralston (1954).

The method of Abell *et alii* (1952) was slightly modified by increasing the temperature for saponification to 65° C.

The method of Brown (1959) was used without modification.

The digitonide procedure was carried out as follows. Serum (0·1 ml.) was incubated with 2·5% alcoholic potash (5·0 ml.) at 65° C. for one hour, and the non-saponifiable lipids were extracted with petroleum ether. This procedure, as well as that for preparation of the internal standards, is given elsewhere (Brown, 1959). The non-saponifiable lipids were redissolved in ethanol–acetone mixture (1:1), and the 3-beta sterol was precipitated with digitonin. In a second and more direct procedure for determination with digitonin, the serum was saponified in alcohol, the hydrolysate was neutralized with acetic acid and diluted with an equal volume of acetone, and after centrifugation samples were again taken for preparation of cholesteryl digitonide. The details of the method for precipitation of the digitonide compounds and its colorimetric determination with the reagent of Abell *et alii* (1952) are described elsewhere (Brown, 1961*b*).

Results.

The results of determination of cholesterol in the serum of 10 male human subjects by the five methods are summarized in Table I. Each value is the mean of three independent determinations except in the digitonide determination, in which each is the mean of two values.

The mean values for each group obtained after saponification did not differ significantly. The data were pooled and tabulated in Table II, where the errors in the method of Zlatkis *et alii* (1953) are shown as percentages of the pooled estimates and as absolute values.

Discussion.

The similarity of the values obtained after saponification confirms the usefulness of the method used in this paper for preparation of the non-saponifiable extract. The mean value obtained by the method of Zlatkis *et alii* (1953), on the other hand, is about 16% higher than the standard value. By coincidence, an error of about this magnitude is found when a number of colorimetric methods for the determination of serum cholesterol level are used without saponification (Brown, 1961*a*). In the method of Zlatkis *et alii* (1953) the error is best expressed in absolute terms as it seems to be independent of the serum cholesterol level and the age of the subject. It is equivalent to 36 mg. per 100 ml. of cholesterol. The widely used method of Bloor (1916) is also often cited as being in error by about 15% (Brown, 1961*a*); but, in this case, the error is proportional to the ratio of cholesterol to cholesterol ester, and a correction factor

related to the total cholesterol level can be used as the ratio is fairly constant (Kenny, 1952). Statistical analysis of the data in this paper also shows that the most representative 95% of the values obtained by the method of Zlatkis *et alii* (1953) for individual serum samples are no less than 14 mg. per 100 ml. above the correct value and no more than 58 mg. per 100 ml. above the correct value.

TABLE I.
Serum Cholesterol Level as Estimated by Five Methods.

Method.	Mean (Mg. per 100 ml.)	Standard Deviation.[1]
Direct procedure:		
Zlatkis *et alii* (1953)	273·8	6·9
On the non-saponifiable extract:		
Abell *et alii* (1952)	237·8	2·7
Brown *et alii* (1959)	239·4	4·5
Digitonide procedure:		
Direct	240·3	5·4
On the non-saponifiable extract	235·6	4·6

[1] For each of three independent determinations (a, b, c) on each of 10 sera

$$\sqrt{\left[a^2+b^2+c^2-\frac{(a+b+c)^2}{3}\right]/20}$$

or two independent determinations in the case of the digitonide estimates

$$\sqrt{\frac{(a-b)^2}{20}}$$

The use of correction factors does not entirely eliminate the confusion caused by the assertion of Zlatkis *et alii* (1953) that their method was as accurate as the digitonide method of Schoenheimer and Sperry (1934). If, for example, 36 mg. per 100 ml. is deducted from the serum cholesterol values obtained by the method of Zlatkis *et alii* (1953) in the comparative study of Australian white and aboriginal subjects by Charnock *et alii* (1959), then they

TABLE II.
Limits of Accuracy in Method for Direct Serum Cholesterol Determination.

Age of Subject (Years).	Values.		Excess Values.	
	Zlatkis *et alii*.	Pooled Standard.	Percentage.	Mg. per 100 ml.
54	279·7	255·3	9·6	24·4
22	211·6	175·4	21	36·2
27	282·3	253·0	12	29·3
23	260·0	237·2	9·6	22·8
37	289·3	259·1	12	30·2
28	203·3	155·8	30	47·5
26	310·3	279·5	11	30·8
37	310·6	273·2	14	37·4
43	364·0	319·0	14	45·0
23	227·3	173·1	31	54·2
Mean[1]	273·8	238·2	16	35·8

[1] The 5% confidence limits for difference between mean estimates for each serum sample by the procedure of Zlatkis *et alii* (1953) and the corresponding standard estimate for the serum was computed from the formula

$$2\sqrt{\frac{\Sigma(x-\bar{x})^2}{9}}=\text{mean}\pm 22 \text{ mg. per 100 ml.}$$

where x=an excess value in column 5.

$\bar{x}$=mean of these excess values.

are more in accord with more accurately determined values for similar ethnic groups, the levels for tribal aborigines then being 176 mg. per 100 ml., for urbanized aborigines 198 mg. per 100 ml., and for white Australians in Adelaide 257 mg. per 100 ml. Nevertheless, even after correction, the value for white male subjects in Alice Springs is 277 mg. per 100 ml. This is higher than the mean value obtained with methods employing saponification for any group of males selected solely according to age and apparent good health (for example, Keys *et alii*, 1958*b*; Lewis *et alii*, 1957; Adlersberg *et alii*, 1956; Bronte Stewart, 1958, Stamler, 1959). It is even higher than that found for people in the west of Finland, where a level of 270 mg. per 100 ml. is associated with an unusually high death rate from coronary disease (Keys *et alii*, 1958*a*). Thus, the reason, whatever this may be, for the high value in Alice Springs is not trivial by epidemiological standards.

It is not possible without repetition of the experiment to decide whether the high value is due to methodological errors, as the correction factors may not be valid in Alice Springs. Nor is there reason to assume that the correction factors apply equally in different races, though it may be noted that similar uncorrected values have been obtained with the same method for serum cholesterol levels in subjects of similar sex, age and race in both Sydney and Adelaide (Schwartz *et alii*, 1957; Charnock *et alii*, 1959; Brown, 1961*a*; and the present paper), and similar values have been obtained for the error in Sydney and in the U.S.A. (Baerts *et alii*, 1956; Brown, 1961*a*). It is, in fact, possible that men in Alice Springs do have very high serum cholesterol levels.

The poor correlation between actual and estimated values obtained by the method of Zlatkis *et alii* (1953) must also reduce the value of the method in establishing correlations between cholesterol levels and other factors. It is possible, for example, that this methodological error was responsible for the lack of relation found between serum cholesterol levels and myocardial infarction in the age-matched and sex-matched subjects examined by Schwartz and Caseley-Smith (1958).

Rather similar difficulties have been created by the method of Bloor (1916). Friedman and Rosenman (1957) pointed out that, though the Neapolitans consumed diets relatively low in animal fats in comparison with people in the U.S.A., the serum cholesterol levels for Neapolitans were similar to those of age-matched and sex-matched American subjects, and that this was contrary to the hypothesis that serum cholesterol levels were related to the consumption of fats. However, the Neapolitan data were obtained with the method of Bloor (1916), which gives values about 15% higher than the methods employing saponification that were used in the American laboratories. Since it had been stated (Keys *et alii*, 1950; Keys *et alii*, 1954) that the method of Bloor (1916) was as accurate as the digitonide procedure of Schoenheimer and Sperry (1934), it is not surprising that some confusion surrounds the hypothesis relating animal fat consumption to serum cholesterol levels and coronary disease, owing merely to errors in analytical chemistry.

The view (Friedman *et alii*, 1958) that "there has not been an increase in serum cholesterol . . . during the last five decades" illustrates a further limitation imposed by the use of inaccurate methods. This statement was based on a variety of published values, among which the highest mean estimates obtained by early investigation were 240 mg. per 100 ml. for women and 220 mg. per 100 ml. for men (Bloor, 1916). Ages were not given, but the subjects were apparently largely young adults. It is difficult to apply the correction of 15% to the data obtained at this time with the method of Bloor (1916), as blood was then usually collected in vessels containing powdered oxalate or citrate, and this must have reduced the values in a rather unpredictable manner (Sperry and Schoenheimer, 1935). The early serum cholesterol values obtained were also rather inconsistent, and Bloor himself on another occasion obtained considerably lower estimates for subjects who were apparently no younger (Bloor and Knudson, 1916). It would seem reasonable to believe that serum cholesterol levels in 1916 in the U.S.A. were high by present world standards, but more definite conclusions are not possible. It was, in fact, dissatisfaction with the early colorimetric techniques of cholesterol determination that led Page *et alii* (1935) to devise a method (based on digitonin precipitation) to obtain data adequate to set a standard for serum cholesterol levels in the U.S.A.

The next comprehensive attempt to determine standard values for serum cholesterol levels in the U.S.A. was due to Keys *et alii* (1950). It appears that the younger

subjects of the study were examined by workers in the Student Health Service using the method of Schoenheimer and Sperry (1934), and that the method of Bloor (1916) was used to obtain the serum cholesterol values in the older age groups. If this was the case, then it is feasible that methodological errors could have been partly responsible for the marked trend found for serum cholesterol values to vary with age. Keys *et alii* (1950) held that rather similar values were obtained by the two methods; but in view of the many contrary views, it was clearly hazardous for the values obtained to be used as the basis for assessing the presence of hypercholesterolæmia in coronary disease in the U.S.A., let alone in other countries (Biörck *et alii*, 1957). Other examples of hazardous comparison of data due to the use of different methods for cholesterol determination may be found (Thompson *et alii*, 1959; Weinred *et alii*, 1957; Harris Jones *et alii*, 1957).

The Cooperative Study on Lipoproteins (Gofman *et alii*, 1956; Lewis *et alii*, 1957) contributed substantially to knowledge on serum cholesterol levels in the U.S.A. This work also demonstrated the difficulty in obtaining reproducible estimates between laboratories even when one method is used, so that there is no doubt that the use of several methods may considerably complicate determination of standard population data (Riven *et alii*, 1958; Page *et alii*, 1957; Morris, 1960). This problem has become more acute in recent years with the publication of an increasing number of methods of questionable accuracy.

With the probable development of coronary disease in communities being industrialized, there is, from the point of view of research, a growing need for accurate data on yearly trends in the levels of cholesterol in serum. So far as the U.S.A. is concerned, it is possible that the determination of Liebermann-Burchard positive matter in the non-saponifiable matter of serum is a highly accurate measure of cholesterol (Abell *et alii*, 1952), except during the use of certain drugs to reduce the synthesis of cholesterol by the liver (Blohm *et alii*, 1959; Steinberg *et alii*, 1960). The data in this paper do not show the content of cholesterol in the Liebermann-Burchard positive matter of serum. However, they suggest that there is no worthwhile advantage to be gained from the use of the complicated digitonide techniques for purification of cholesterol prior to its determination with Liebermann-Burchard reagent, at least so far as white Australian subjects are concerned. However, it should be recognized that only a few relevant studies have been made on civilized peoples and practically none on primitive peoples.

Cholesterol is not the only sterol found in serum. Some 3-beta hydroxysteroids other than cholesterol (for example, cholestanol—Beher *et alii*, 1957) are atherogenic, and population values for total 3-beta hydroxysteroids may be more relevant to studies on coronary disease than values for pure serum cholesterol. Indeed, Greig and Cook (1960) found cholestanol and other 3-beta hydroxysteroids in the serum of British subjects which were not Liebermann-Burchard positive. The significance of values for the levels of these sterols in serum may prove to be slight; but it should be none the less clear that more work is required to confirm the accuracy of methods for determining atherogenic sterols in epidemiological studies on coronary disease.

Conclusions.

The error in the most popular "direct" method for serum cholesterol determination was found to be 36 mg. per 100 ml. for a group of subjects in Sydney. It was independent of the serum cholesterol level. Individual estimates did not correlate well with correct values. Examples are cited to demonstrate the confusion in epidemiological studies on coronary disease owing to inaccurate determination of the serum cholesterol level. The limitations of correction factors are discussed. Determination of cholesterol in the non-saponifiable extract is advocated so that data obtained in different laboratories may be compared directly.

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HERPES SIMPLEX INFECTIONS OF THE MOUTH.

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WHILE frequent references to herpes simplex infections of the mouth are seen in the dental literature, such references are rare in the medical literature. Because my colleagues and I have seen an appreciable number of misdiagnosed or undiagnosed cases of herpetic stomatitis, it is the object of this paper to discuss the symptoms, signs, histopathology, diagnosis and treatment of this infection in an attempt to make its recognition more obvious.

The herpes simplex virus, causative microorganism in this infection, has a particle size of about 100 mμ by filtration methods (Elford, Perdraw and Smith, 1933). It has a predilection for epithelial tissues, where it is associated with intraepithelial vesiculation. After the initial infection, the virus remains latent in the epithelial tissues, particularly at muco-epithelial junctions, to be activated at a later stage by various stimuli. Primary infections and exacerbations are therefore recognized, and these, although having a basically similar vesicular lesion, differ considerably in the severity of general symptoms and local signs. The herpes simplex lesion is defined as "an active eruptive disorder, characterised by the appearance of grouped vesicles on a mildly inflammatory base, accompanied by sensations of heat and burning, and usually occurring about the face and genitalia" (Ormsby and Montgomery, 1954).

The primary acute oral infection has a definite clinical picture and is described as acute herpetic stomatitis. It is probably the most common type of oral infection occurring in children, and is most often seen in children aged between 18 months and four years.

A clinical survey showed that 70% of primary infections occur in patients under six years of age and 40% were found to occur under three years of age (Scott, Steigman and Convey, 1941). Male and female children appear to be equally affected. Ten to fifteen *per centum* are either adolescents or adults when they first experience this infection of the mouth. The remainder of the population are never infected, and it is suggested that they have a resistance, which is, however, not an immunological one (Burnet and Williams, 1939). Various workers (Burnet and Williams, 1939; Andrewes and Carmichael, 1930) have shown that there is a greater incidence of herpetic infections in persons from poorer class homes. Secondary bacterial infection, often by streptococci, frequently complicates the clinical picture of primary herpetic stomatitis and it is suggested that the condition known as streptococcal stomatitis or streptococcal gingivitis is a secondary infection by streptococci of lesions caused by the herpes simplex virus.

The clinical picture of the primary infection is more severe in adults than in children. While in adults it is common for the infection to follow, or nearly coincide with, debilitating conditions such as respiratory diseases and periods of stress or personal neglect, it is common for the infection to occur in apparently healthy children. However, with children, a history of contact with other children suffering from a herpetic infection, whether primary or recurrent, is often elicited. Hence it is not uncommon to find this infection occurring in small epidemic proportions. The writer has observed on a number of occasions, when examining groups of school children, the very high incidence of herpes labialis at about the same stage of development. It is also common to find children in the same family suffering from the condition concurrently, often with the history of the infection occurring first in one child who had been in contact with other infected children. The highly contagious nature of the infection therefore explains its widespread incidence and the fact that it is one of man's most common diseases. Burnet and Williams (1939) demonstrated the presence of the virus in the saliva of patients with acute lesions, and the ease of autogenous infection and of transmission from child to child by fomites can therefore be explained. The primary infection occurs in persons who have no circulating antibodies specific for the herpes simplex virus, and has an incubation period of from three to nine days (Scott, Steigman and Convey, 1941).

The condition first appears as an illness somewhat similar to a severe cold or influenza. A sore throat is often the first symptom. Clusters of thin-walled vesicles on an erythematous mucous membrane or on the skin, and distributed in or about the mouth, appear about a day later. They may occur anywhere on the oral soft tissues (herpetic stomatitis) and may include the gingivæ (herpetic gingivostomatitis). They may occur on the face (herpes facialis), on the lips, particularly the lower one (herpes labialis) or on the chin (herpes mentalis). Any combination of these may be seen at the one time. Because the vesicles are intraepithelial, and therefore fragile, they are not often observed. They are most frequently straw-coloured, varying from about 1 to 3 mm. in diameter, and contain a clear fluid from which the herpes simplex virus can be isolated. They may remain intact for six to 12 hours only, and once they rupture they appear as groups of small erosions, covered at first by a cream-coloured membrane or tag, which is the collapsed roof of the vesicle. Secondary infection by commensals soon occurs and shallow ulcerations result. This secondary infection causes the ulcers to extend, and they soon coalesce to produce a larger, deeper, more painful ulcer with a raised, red, micropolycyclic edge and a depressed, yellow or grey-white, slough-covered floor. These lesions are most commonly seen on the lips, the margins of the tongue, the buccal and sublingual mucosa and the palate, and less commonly on the gingivæ. Often the gingivæ are considerably enlarged by

an inflammatory œdema so that the gum may cover more than half the clinical crowns of the teeth. They have then a typical ham-pink coloration due to hyperæmia, are tender to palpation and bleed readily. Ulceration is frequently not extensive on the gingivæ, although a ragged gingival margin is often present (Figure I). On other

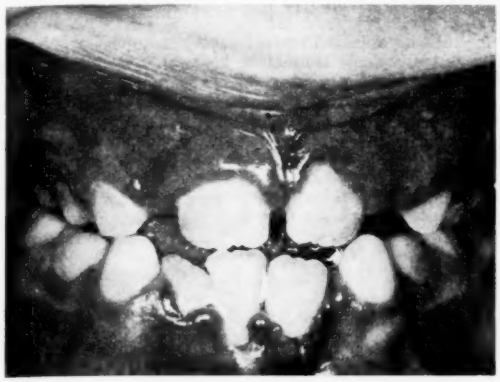

FIGURE I.
Primary herpetic stomatitis in a child showing an œdematous gingiva and a ragged gingival margin.

occasions the only gingival signs present may be a thin, red line around the necks of the incisor teeth. Sialorrhœa, submandibular and cervical lymphadenopathy and straw-coloured crusts on the lips are commonly exhibited. Eating is painful and difficult, necessitating careful attention to diet. Symptoms of toxicity—malaise, pyrexia, tachypnœa and tachycardia—are relatively marked in the adult. A pyrexia of 102° F. is often observed in children, while adults may have a fever as high as 105° F. and be prostrated for several days as a consequence. The course of this disease is limited, and with or without treatment lasts 10 to 14 days. A diffuse erythema and œdema remain for a few days after the ulcerations have healed. Because of the superficial nature of the ulceration scarring does not generally follow resolution.

While complications are rare, the herpes simplex virus may cause an encephalitis, an infection of the mucous membrane of the eyes and genitalia, and autoinfection of the thumb, fingers or arm by a sucking habit, and is known to precede other virus diseases, such as infectious mononucleosis (Nathanson and Monin, 1953). A common finding in adults during a later stage of the infection is a pericoronitis involving the operculum over an impacted or partly-erupted lower third molar.

Recurrent infections are uncommon (Cooke, 1950), while recurrent exacerbations occur commonly in individuals who have suffered a primary infection, and who therefore have circulating antibodies which are specific for the herpes simplex virus. The virus may be stimulated to activity from its latent state in the epithelial cells by various relatively minor stimuli, such as sunburn and trauma from dental procedures (for example, at the site of a local anæsthetic injection) (Figure II), and during debilitated states (for example, a "cold sore" often seen in association with a common cold) (Figure III). It is considered that this reactivation of the virus is due to a change in resistance of the host rather than an autogenous or heterogenous reinfection. The lesions in the recurrent form of the disease are essentially the same as those seen in the primary infection, the main exception being that the recurrences occur in a localized area, most frequently on the lips as "cold sores", and are not usually accompanied by general signs and symptoms. The vesicles are seen sometimes within hours of a traumatic incident and usually within two days. The vesiculation is frequently preceded by prodromal symptoms of a burning or itching sensation and diffuse erythema of the localized area to be involved. Soon a small cluster of vesicles erupt on this patch of erythematous mucous membrane. Submandibular and cervical lymph nodes are frequently enlarged and tender to palpation, while general symptoms of malaise and pyrexia are commonly absent. Although observations do not always bear this out, it is claimed that recurrent lesions do not reappear in exactly the same place, and it is thereby suggested that a local tissue immunity is conferred on a site following a previous infection.

FIGURE II.
A group of herpetic erosions at the site of a local anæsthetic injection in the palate have coalesced to produce an ulcer with a micropolycyclic outline.

FIGURE III.
Herpetic vesicles at the mucoepithelial junction of the lip in a child with a severe cold. There were no other herpetic lesions.

The essential histopathological lesion caused by the herpes simplex virus is an intraepithelial vesiculation produced by intra- and extracellular œdema and degeneration of the epithelial cells. The epithelial cells in the vicinity of the basal layer swell, take on a rounded form, lose their intercellular bridges and separate from one another (Figure IV). This has been described by Cooke (1960) and Cahn (1950) as "ballooning degeneration", and leads to fragmentation of the epithelial cells with consequent vesicle formation. The nuclei of some of the affected epithelial cells may undergo mitotic division to produce multinucleated cells. These are the so-called "epithelial giant cells" or "balloon cells", which are considered to be diagnostic features of a herpes simplex infection (Cooke,

1958), but which also occur in herpes zoster, variola and varicella (Lever, 1950). Nuclei of other cells may degenerate, lose their staining property and disintegrate. The vesicle in this condition is a fluid-filled cavity amongst the epithelial cells. The roof of the vesicle is formed by compressed layers of epithelium, while the floor is formed by œdematous cells of the basal-cell layer. In close proximity to the vesicle, epithelial cells with intranuclear inclusion bodies of Lipschutz are sometimes found (Lipschutz, 1921; Nicolay and Kopciowski, 1938). These inclusion bodies are eosinophilic and rounded, and are considered variously to be colonies of virus, degenerated remnants of the affected cell or a combination of both of these (Nicolay and Kopciowski, 1938). The presence of these eosinophilic intranuclear inclusion bodies is pathognomonic of a virus infection. The inflammatory infiltration seen in the papillary layer is mainly lymphocytic.

onto the freshly-scarified cornea of a rabbit's eye. The rabbit develops an acute keratitis in three to four days and will often die about 10 days later from a central nervous system infection. Typical herpetic vesicles develop on the scarified cornea. Scrapings from these corneal lesions exhibit "balloon cells" and the inclusion bodies first described by Lipschutz (1921). Experience in using this technique suggests that a negative result is of little value, while positive evidence is of diagnostic significance.

The microscopic evidence in biopsy material of eosinophilic intranuclear inclusion bodies, multinucleated epithelial cells and ballooning degeneration of the epithelium in relation to the basal layer is claimed to provide positive diagnostic evidence of a lesion caused by the herpes simplex virus (Glickman, 1958). However, this claim is not substantiated, for an indistinguishable histopathological picture is seen in herpes zoster, variola and varicella (Lever, 1950).

FIGURE IV.

Photomicrograph of biopsy showing an intact vesicle which occurred on a lip. Ballooning degeneration of the epithelial cells at the base of the vesicle is evident. There is a subepithelial infiltration of inflammatory cells (× 90).

While the diagnosis of herpes simplex infections in and around the oral cavity can most often be readily established from the patient's history and clinical presentation, it may be necessary to make use of special examinations for confirmation. The special examinations which help most in confirming the clinical diagnosis are the Tzanc test, the Paul test, biopsy, estimation of the specific antibody titre of the patient's serum during and after the infection, and the identification of the organism after isolation on the chorio-allantoic membrane of a chick embryo with the aid of an electron microscope.

The Tzanc test is performed as follows. If the vesicle is intact its roof is removed and the base is scraped with a sharp instrument. If the vesicle has ruptured the base is scraped in a similar way and the material obtained is smeared on a glass slide, fixed and stained with a polychromatic stain. Microscopic examination of this stained smear will reveal characteristic multinucleated epithelial giant cells which are considered to be pathognomonic (Tzanck, 1949). Lever (1950) described these cells as occurring in vesicular lesions caused by other viruses, and the test therefore is only of significance if related to the clinical presentation. The absence of the pathognomonic features in cases indistinguishable clinically from recurrent herpes simplex has been noticed by the writer and has been commented upon in the literature.

For the Paul test, fluid is removed from a suspected herpetic vesicle with a micropipette. This fluid is flowed

There is no evidence of circulating specific antibodies at the commencement of primary herpetic stomatitis. However, as successive titrations are carried out during the course of the infection and during convalescence the specific antibody titre rises and remains permanently at a high level. Titrations made at the commencement of and during recurrent herpetic attacks will demonstrate that there is a high specific antibody titre at the beginning of the infection which rises slightly during the course of the infection and during convalescence, and is said to remain at a high level (Glickman, 1958), although this cannot always be demonstrated.

Fluid removed with a micropipette from an intact herpetic vesicle should contain the herpes simplex virus. From this fluid the virus can on some occasions be grown on the chorio-allantoic membrane of a ten-day incubated fertile fowl's egg (Burnet, 1936). After the membrane has been seeded, the egg is incubated for another two days before the membrane is harvested. The membrane is then inspected, for pocks of the herpes simplex virus (Figure V). This test also is equivocal. A positive result is of diagnostic significance, but absence of pocks does not necessarily indicate the absence of the virus in the vesicle fluid.

Acute herpetic stomatitis is confused most often with acute necrotizing ulcerative gingivitis (Vincent's infec-

tion), to which it bears very little resemblance. These infections may occur concurrently and make clinical recognition initially difficult. While the general symptoms of malaise, pyrexia and halitosis are common, and the submandibular lymph nodes are enlarged and tender to palpation, the intraoral signs and the course of the infections are virtually opposites. Primary herpetic lesions occur most commonly in young children, are self-limiting, commence as groups of vesicles anywhere on the oral soft tissues, but often avoiding the gingivæ, and result in confluent ulcers which heal without scarring. Acute necrotizing ulcerative gingivitis, on the other hand, is extremely rare in children under 15 years of age, is related particularly to the interdental papilla, commences as an ulcer, is not self-limiting, is a destructive lesion and is thought to be caused by a spirochæte-bacterioid infection. Acute herpetic stomatitis needs also to be differentially diagnosed from erythema multiforme, varicella, variola, herpes zoster, pemphigus, various allergic manifestations, bullous lichen planus, oral aphthæ, agranulocytosis, aplastic anæmia and desquamative gingivosis.

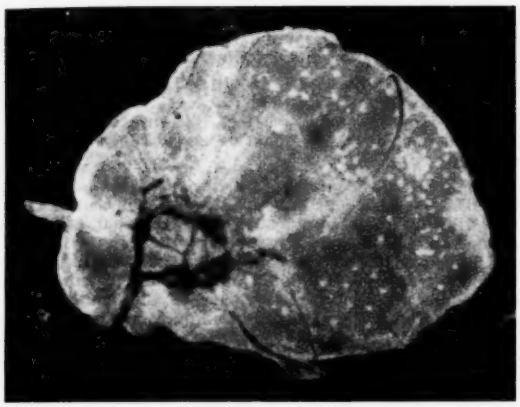

FIGURE V.
A harvested chorio-allantoic membrane showing numerous pocks of the herpes simplex virus (× 5).

Erythema multiforme localized to the oral mucosa and lips may present a diagnostic problem, but this condition frequently occurs with widespread skin and mucous membrane lesions of typical pattern, and diagnosis is thereby assisted. The characteristic iris lesion of the skin is caused by central resolution of a papule. It is not uncommon for erythema multiforme to persist for many weeks, but herpetic stomatitis runs a self-limiting course of about 10 to 14 days. The lesions are frequently hæmorrhagic and this is exemplified in the region of the mouth by blood-stained, encrusted lips.

Variola, varicella and herpes zoster are caused by viruses, and while there is a similarity in vesicle formation and histopathology between these conditions and herpes simplex infections, herpes zoster is rarely bilateral, being confined to the sensory distribution of the affected nerve, and frequently associated with considerable, relatively widespread pain. Variola and varicella can most often be diagnosed by history and clinical appearance.

In pemphigus the constitutional symptoms are often severe and the bullæ, frequently occurring in small numbers, are present on an otherwise normal-appearing mucous membrane. A positive Nikolsky sign is obtained, and acantholytic cells are present in scrapings from the floor of the lesion. Allergic manifestations of a vesicular nature can usually be excluded by the history. Bullous lichen planus has a characteristic histopathological appearance distinct from that seen in herpes simplex infections. The typical white-patterned keratotic lesions which commonly accompany the bullæ of lichen planus in the mouth, and, in a large proportion of cases, the presence of associated skin lesions, usually make it possible to differentiate clinically between this condition and herpetic stomatitis.

Oral aphthæ are ulcers which themselves present a diagnostic puzzle, but which, because of differences in clinical presentation and histopathology, should not be confused with herpetic ulcerations. Oral aphthæ have raised, red, ragged edges, rarely occur in numbers greater than five, and most commonly occur on the vestibular mucosa and floor of the mouth. They do not commence as a vesicle, but rather as a red, irritating nodule. They are exquisitely painful, and have no associated lymphadenopathy or general symptoms unless extremely severe. In the recurrent form they usually occur more frequently, and with more periodicity, than recurrent herpetic ulcerations. Because they are deeper ulcers they frequently heal with scarring. The histopathology shows a non-specific ulcer which extends deeper into the corium than is seen in herpes simplex lesions. There is no evidence of balloon cells, inclusion bodies or circulating antibodies specific for the herpes simplex virus (Stork, Kibbrick and Weisberger, 1954).

The blood dyscrasias, agranulocytosis and aplastic anæmia, can easily be confused in the early stages with primary herpetic stomatitis when the vesicle stage of this latter condition has not been observed. However, if doubt as to the cause of the ulceration exists, a blood examination, including a differential white-cell count, will put the diagnosis beyond doubt.

Desquamative gingivosis (Engel, Ray and Orban, 1950), basically a degenerative condition of the gingival epithelium, appears clinically as varying degrees of epithelial desquamation of the gingivæ with subsequent reddened patches. These lesions bear little similarity to a herpes simplex infection of the oral tissues. There are no vesicles and no acute symptoms in this chronic, non-limiting condition. Subepithelial lesions resulting in separation of the epithelium are seen when biopsy material is examined microscopically (Cahn, 1941).

The treatment of primary acute herpetic stomatitis is essentially symptomatic and supportive. General treatment should be directed towards rest, maintenance of fluid balance, provision of adequate nutriments and the control of pain and fever. Local treatment is designed to combat secondary infection of the initial erosions. No drug at present available will dramatically shorten the 10 to 14 day course of the disease. A mouth wash of aureomycin in 2% solution, used six-hourly for the first three to four days considerably reduces the pain and limits the secondary infection in severe cases, especially adults. In the less severe cases in children and adults, and after the first few days of the severe infection, aqueous gentian violet in 1% solution applied to the ulcers at least after each meal reduces the pain, and makes mastication tolerable. Recurrent herpetic infections have been treated successfully by the intradermal use of smallpox vaccine, while attempts to immunize against the herpes simplex virus by the use of various strains of herpes simplex vaccines have not been successful (Savitt and Ayers, 1949). It is now considered prudent to use influenza A and B vaccine to avoid the possibility of an encephalitis produced by cowpox vaccine (Cooke, 1956). The administration of large doses of B complex vitamins or brewer's yeast has effected a temporary remission in some recurrent cases and in others has increased the time between recurrences. As in the acute form, gentian violet is a reasonably successful palliative.

In an attempt to help with the understanding of this well-documented infection the oral lesions caused by the herpes simplex virus have been described and the signs and symptoms, histopathology, diagnosis and treatment have been discussed.

Acknowledgement.

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ADVANCES IN THE ANATOMY AND EMBRYOLOGY OF THE LYMPHATIC SYSTEM AND THEIR APPLICATIONS.

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IT is not necessary to emulate "The Physician" who "went into wild ecstatics when I showed him my lymphatics" in order to stress the importance of a thorough knowledge of the anatomy of the lymphatic system to the pathologist and clincian alike.

Most textbooks on anatomy give a description of the lymphatic system which has not been completely revised since Leaf translated the work of Poirier and Cuneo in 1903, and it is upon this work that most of our scanty descriptions depend. It is largely due to the difficulty of dissection of these small vessels, as well as the unsatisfactory techniques of the past, that this important branch of human anatomy is omitted in detail from our textbooks. These omissions prompted Drinker (1942) to write: "There are few people even today who have ever really seen lymphatics, and usually even such persons have had to be content with a fleeting view of none save the most conspicuous part of this vasculature."

History.

According to the writings of Galen in A.D. 168 it appears that Aristotle, Herophilus and Herastistratus in the second and third centuries B.C. all saw lymphatic vessels but confused them with small arteries and veins. In the sixteenth century Eustachius first recognized and described the thoracic duct in the horse, but thought it was a "white vein" and described it as the "vena alba thoracis".

In 1622 Aselli, who was professor of anatomy and surgery at Pavia, became most enthusiastic about a number of "white cords" in the mesentery of a well-fed dog. He traced them from "almost innumerable beginnings" to their termination in a receptaculum. He thought at first they were nerves, but soon changed his mind when he found a "milky fluid gushed forth" when they were punctured. Indeed it was Aselli who first realized that here was a system of vessels quite separate from the blood vessels and containing a different fluid. Only a few notes of his were ever published after his death and it is not clear if he appreciated that each organ had its lymphatic drainage or what he thought this fluid really was. At any rate Aselli can be said to be the father of the lymphatics, who first recognized them as such.

Thomas Bartholin, the father of the better known Caspar Bartholin of glandular fame, first used the term lymphatics in 1660, but it is not clear from his descriptions whether he appreciated them as a system of vessels separate from veins and capillaries.

During the eighteenth century Hewson, Cruikshank and Meckel all made advances into this new system, and William Hunter shortly before his death in 1783 had come to regard the lymphatics as a "child of his own intellect".

Sappey (1847) commenced a series of investigations in which he succeeded in injecting the lymphatics with water, thus dilating them up to such a degree that he was able to map out the larger, unruptured ones. Later he devised and improved a technique of mercurial injections from which he was able to publish an atlas of the lymph vessels and glands in almost every part of the body. The subareolar lymph plexus bears his name in modern textbooks.

Poirier, Cuneo and Delamere (1892) remapped the lymphatic system in greater detail than Sappey had done. This had been made possible by the improved injection technique with prussian blue injection-mass mixed with cinnabar and "absolute black". So valuable was this work that Leaf (1903) translated it into English.

It is to Jamieson and Dobson (1910) that we owe a further improvement of this Gerota technique, as it is called, of which a more detailed account is given below. They gave the first lucid description of the intrinsic lymph vessels of the tongue using full-term fœtuses as their material.

Sabin (1911), in the United States of America, expelled any doubt about the systemic nature of the lymph circulation, for she traced the development of these vessels from early localized "lymph sacs", from which a closed tubular system of vessels was established and which had no communication whatever with blood vessels.

In the past 20 years probably no investigators have done more pioneering into this neglected system than Drinker and Yoffey (1941). Their work is cited in almost every communication, whether it be physiological, histological or anatomical.

Modern Methods of Examining the Lymphatics.

The most convenient way of examining the lymphatics is to lounge in a comfortable armchair and to watch the excellent film prepared by Dr. R. L. Webb of Illinois University entitled "Mesenteric lymphatics, their nature and behaviour in the living rat". But the more difficult a task becomes, the more satisfaction there is to be derived from attempting it with gradual improvement in technique until at length success is attained. It is obvious that to demonstrate the smallest of these vessels we must distend them to their maximum extent with some contrasting medium which will not damage or penetrate their walls. These tiny vessels will then be dissected, fixed and mounted. It would be useless here to review the large variety of techniques used, from Sappey's water

injection to Florey's "Hydrokollag" demonstration of diaphragmatic lymphatics, or the most recent lymphangiogram of Pinto (1946) using "Tordiol". But it is of value to consider the method of Gerota (1896) using a filtered mixture of prussian blue, turpentine and sulphuric ether, for this is the most frequently used injection-mass today and is capable of showing all but the very smallest lymph vessels. Since this mass is injected under low pressure the vessel walls are not ruptured, as was the case with mercurial injections. Jamieson and Dobson (1910) injected the Gerota mixture with a simple apparatus consisting of an air pump, a glass jar for the mixture, and a fine platino-iridium needle. Particulate matter such as india ink, when injected into small vessels, caused an obstruction to their lumina. Therefore Drinker and Churchill (1927) employed a stable suspension of very fine graphite particles known as "Hydrokollag", which does not precipitate in the presence of organic fluids and therefore did not obstruct the smallest vessels. The lymphatics of the tongue, the lips, the diaphragm and the pinna were investigated in this way.

Pierce (1944) used a 1% solution of trypan blue in a 3·5% solution of saline to inject the renal artery of an anæsthetized dog. The subcapsular plexus in the kidney was well demonstrated by this method, but the efferent lymphatics from it into the perinephric fat were not visible, probably owing to obstruction with particulate matter. Sappey (1847) first demonstrated these important efferents of the kidney by water injections, and every surgeon is well aware of their existence.

More recently Pinto (1946), of Oporto University, reported that he successfully injected a radioopaque medium into one of the larger efferents of the popliteal glands of a dog using a strong, metal-ringed glass syringe after careful dissection of the fossa. The medium he used was "Tordiol", a thorium derivate, which precipitates slowly when in contact with organic fluids and will therefore adhere to vessel walls rendering them radioopaque for longer periods than will "Thorotrast", "Abrodil" or "Perabrodil". It is mixed with a 5% solution of ethyl alcohol in the proportion of 2:1 to lessen its viscosity, but even so its precipitation is liable to block even a medium-sized vessel. Nevertheless Professor Pinto obtained lymphangiograms of the iliac and lumbar nodes in this way.

Pathological Applications.

It is unfortunate that the importance of the anatomy of the lymphatics is so often not realized by students until they have embarked upon clinical medicine and surgery. Indeed, it is the frequent lament of clinical and pathology teachers that lymphatic drainage of important viscera finds no pigeon-hole in the memories of final-year students. "What do they teach you in that anatomy department?" is frequently heard at the bedside. If this important system is dealt with in small print only and brief paragraphs in Cunningham's "Manual of Practical Anatomy", and only 35 pages out of the 1604 pages in the most recent edition of Gray's "Anatomy" are considered necessary on the whole system, there need be no amazement that the lymphatics and their glands are the unwanted children of second- and third-year students.

For these reasons it may be advantageous to review just a few of the pathological conditions in which the anatomy of the lymphatic system plays a leading part.

Malignant Neoplasms.

With regard to metastatic spread of neoplasms, Sampson Handley's view was accepted for a number of years. He showed that there was a gradual growth of "cords" of malignant cells which "permeated" along the lymphatics outwards from the primary growth. This permeation of the malignant cells into neighbouring tissues was based upon Handley's conception of the anatomical segmentation of lymphatics from a localized area of skin or mucosa. The result was that an area of "neoplastic ringworm" was produced, which gradually increased in diameter irrespective of the direction of the flow of lymph. Handley showed much clinical evidence in support of his view, but he failed to demonstrate the obliteration of the lymphatics near the primary growth as he had suggested; and there was a suspicion that he confused tissue spaces with lymphatics. More important still was the fact that the same microscopic types of growth—for example, adenocarcinoma—in different regions of the body failed to show the same type of "permeating" spread along the lymphatics as Handley had demonstrated in the breast. No general rule could therefore be accepted on these lines.

The fact that a viscus is known to pour its lymph drainage into certain nearby nodes is no criterion that these nodes may be involved in malignant spread. Alternate routes to the more distant glands may have been the course of the malignant cells. The spread of carcinoma of the rectum is interesting, inasmuch as lymphatic spread can be demonstrated in some 50% only of specimens removed at operation. The submucous plexus of the rectum does not form a continuous lake of lymphatics, but rather a series of segmental arborizations, each with its own separate trunk leading into the retrorectal sinus with its lymph slowly passing upwards into the superior rectal and inferior mesenteric nodes. The size or even the presence of this retro-rectal sinus is often not appreciated, yet it is the main rectal lymph-collecting channel—a veritable receptaculum chyli. Indeed its presence accounts for the upward spread of the metastases even from the lower part of the rectum, and possibly for the slow embolic spread of the malignant cells within the almost static lymph stream.

Spread of Infection.

Although Weed (1914) showed that the cervical lymph nodes could be injected with a ferrocyanide mixture from the intracranial subarachnoid space. Drinker and Yoffey (1941) on the other hand have demonstrated that an injection into the olfactory perineural spaces from the nasopharynx fails to reach the subarachnoid space. They say that this is due to a mechanical obstruction by the perineurium being pushed against the nerve fili. These findings have, of course, an important bearing upon the spread of bacteria and viruses from the nasal mucosa, for it was hitherto believed that the viruses of poliomyelitis and encephalitis reached the intracranial tissues via these perineural spaces traversing the cribriform plate of the ethmoid bone. Indeed Yoffey and Sullivan (1939) have found no viruses of poliomyelitis either in the cervical nodes or in the thoracic duct of rabbits after repeated inoculations into the nasal mucosa. The reasons for this become more apparent when one considers the anatomy of the two mucosal lymphatic plexuses: (i) the intramucosal plexus lying within the mucosa and draining in a direction parallel with the mucosal surface; and (ii) the submucosal plexus lying within the submucous connective tissue and normally having little or no anatomical communication with the intramucosal plexus. It is only when the mucosa becomes œdematous and turgid from inflammatory processes with lowered resistance that the intramucosal lymphatics dilate and open up fresh vessels of communication with the submucosal plexus. Under these conditions we have a flooding of the lymphatic system with the organisms harbouring in the nasopharynx—thus it would seem that the repeated experiments of Yoffey and Sullivan failed to produce a condition comparable with the process which occurs in man.

The spread of the tubercle bacillus within the kidney by the intrarenal lymphatics is another example of lymphatic dissemination. But the "blood-stream *versus* lymphatic spread" of genito-urinary tuberculosis is a war which has raged for many a long year. It was first shown by Thompson Walker that the initial lesion in the kidney is a microscopic subcapsular one which heals as quickly as a fresh lesion appears from continuous blood-stream infection from the lungs. Eventually tissue resistance may be broken down and some of the bacilli find their way into the tubules and the urine as periodic showers of tuberculous bacilluria. The process proceeds until more and more peritubular lymphatics are involved and the first naked-eye lesion appears at the apex of a renal

pyramid. Thus a massive intrarenal tuberculous lymphangitis has occurred before any medullary ulceration and caseation have taken place. Bladder involvement is most easily accounted for by the infection of the urine which has carried the organisms directly to the bladder; nevertheless, intramucosal lymphatic infection can nearly always be found and there is no regional lymph node involvement until the submucous plexus of the ureter has been invaded. A similar process most probably extends down the intradeferential plexus, but the fact that the epididymis is often involved without bladder lesions suggests that an independent blood-stream infection has occurred.

Œdema.

Lymphatic œdema and its production is so controversial a subject that few students—qualified or unqualified—would care to enter the lists in determined defence of their opinions on the matter. It is a subject which cannot lend itself to dogma, at any rate according to the present state of our knowledge.

It appears that a "true lymphatic œdema" can only occur provided all the lymphatics and all their collaterals draining a part are completely obstructed. This is so rare that it was denied by Cohnheim as a clinical entity; nevertheless as Reichart has shown, such œdema can occur before obstructed or damaged lymphatics have regenerated. Hence the majority of these obstructions must be accompanied by some transient infection which not only alters the permeability of the endothelium, but also impairs its proliferation to such an extent that the increased amount of highly proteinized tissue fluid from the capillaries cannot be drained away by the obstructed lymphatics. Those collateral lymphatics that have not been obstructed have an additional load placed upon them, and their drainage powers may be further embarrassed by fibrinous deposits from protein-rich tissue fluid around them. This mechanism in itself is not sufficient to produce the brawny induration of elephantiasis for in the early stages the œdema subsides; but when recurrent attacks of inflammation occur within the devitalized tissues it is then that the collateral lymphatics cannot keep pace with the increasing lymphatic occlusion with each succeeding attack. More fibrinous deposits give rise to the "solid œdema" of the tissue spaces. Extensive resection of regional lymph nodes, and *peau d'orange* may be cited as examples of similar obstructions aided by fibrinous or malignant deposits around over-worked collaterals.

Several ingenious applications of the anatomy of the lymphatics have found their way into surgical attempts to relieve these obstructions. Kondoleon, a Greek surgeon, believed that if communication could be established between the distended tissue spaces more superficially and the deep lymphatics not yet obstructed, then the excess fluid could be drained away in the early stages. By an extensive resection of the deep fascia he allowed the skin to fall against the muscles, thus hoping for a proliferation of any deep lymphatics. The trouble was that the fibrinous deposit extended around the deep lymphatics as well as the superficial ones after the excision, and unless the operation was performed in the very early stages there were not sufficient lymph vessels left patent. Sistrunk performed a more extensive excision of deep fascia, while Sampson Handley threaded pieces of very fine silk from œdematous subcutaneous tissue to normal deeper tissue, believing that tissue fluid would drain along the thread and that lymphatics would be stimulated to regenerate. None of these procedures has met with outstanding success, yet the importance of appreciation of lymphatic geography is exemplified.

Congenital Abnormalities.

The work of Florence Sabin (1902) has been the greatest contribution to our knowledge today of the development of the lymphatic system. She has found that at the 11 mm. stage (sixth week) a capillary plexus becomes cut off from the primitive jugular veins. These isolated capillaries, Sabin states, are the *Anlage* of the lymphatic system, for they gradually dilate and later coalesce to form separate endothelial-lined sacs known as jugular lymph sacs. Later they extend into the upper limb buds.

At the 17 mm. stage (seventh week) these sacs begin to show peripheral buds, which later become cords, and later still fully-canalized vessels. The sacs themselves become segmented, possibly by encroachment of connective tissue strands upon them, until they are eventually broken up into a lymphatic plexus. Simultaneously the outgrowths from the sacs increase in size in a cephalad direction to form the superficial lymphatics of the head and neck.

During the eighth and ninth weeks three other lymph sacs develop in similar manner from veins in the abdomen and primitive pelvis. These are (i) the retroperitoneal sac, which sends buds ventrally into the developing mesentery; (ii) the posterior sac at the junction of the pelvic veins, showing outgrowths into the hindlimb buds; (iii) the cysterna chyli sac, from which grow out lumbar lymph trunks at the caudal end of the thoracic duct, which join up with the outgrowths from the jugular sacs.

It follows from these conceptions that there can be no definite limit to the development of these lymph sacs. Any number of large or small adventitious lymph sacs may be formed from a cut-off capillary plexus. Some may persist while others may retrogress, being obliterated by segmentation of rapidly proliferating mesenchyme around them. Yet other sacs may sprout rapidly and develop lymph channels with wide lumina, soon anastomosing with each other. Such variations in development are the probable explanation of the types of lymphangiomata. A localized dilatation of some of these proliferating vessels, probably caused by obstruction by surrounding mesenchyme, may give rise to the capillary lymphangioma of the skin or the mucosa. Perhaps a larger area of lymphatic vessels becomes isolated from the rest of the outgrowths from the lymph sac by more rapidly proliferating mesenchyme. This results in a more generalized lymphatic dilatation striving to escape from its prison. Macrocheilia or macroglossia results.

Very occasionally a large lymph sac persists, and outgrowths from it are halted, or an adventitious sac develops from it which persists and fails to join up with the rest of the outgrowing plexus. Either of these conditions seems to be the most probable explanation of the multilocular cystic lymphangioma found in the axilla, the root of the neck, the groin, the mesentery and the posterior abdominal wall—that is, in those areas of "lymphatic origin."

The origin of the cystic hygroma appearing soon after birth and in early childhood could be explained in the same way as the other cystic lymphoid swellings. However, it would appear more probable that, owing to their size and invasive properties, they have been derived from ectopic portions of a jugular lymph sac—sequestrations of lymphatic endothelium which have decided to form a lymph sac on their own account. Goetsch (1938) showed histologically that this ectopic tissue retains its power of growth and penetrates into the surrounding mesenchyme as cords, which later canalize and dilate to large extent, producing more and more cystic spaces with similar powers of propagation. The infiltrating edge of such a tumour injures and finally destroys, not only muscle fibres and fatty tissue, but also vessels and nerves. Connective tissue within the cysts finally shows hydropic degeneration and fragmentation, which add to the amorphous content of the multilocular cysts. Indeed we have here a lymph sac which has run amok.

Such then are the extensive ramifications into which the anatomy of the lymphatic system may be turned. It is impossible in a short paper on so general a subject to be complete, either in a review of the investigations or in a sketch of the pathological applications. But it must be apparent that such factors as defensive mechanisms against infection, repair of wounds, production of lymph and the disorders of the reticulo-endothelial system are all members of the huge lymphatic family with which we live. These tiny vessels are canals along which malignant

cells, organisms and their toxins may pass without a passport; the toll is often paid by the patient who owns these canals. The lymph glands are indeed the glands of destiny.

Summary.

1. The history of the advance in the knowledge of the lymphatic system is briefly reviewed from the time of Galen.

2. The more modern methods of examining the lymphatics are briefly described with special reference to Gerota's technique with prussian blue mixture, Drinker and Churchill's "Hydrokollag", Pierce's trypan blue injection of the kidney and Pinto's lymphangiogram.

3. The more important pathological applications of the anatomy of the lymphatic system are sketched. They include the spread of malignant disease, the dissemination of infection through the nasal mucosa and in the genito-urinary tract and the production of œdema. Following a sketch of the embryology of the lymphatic system, the pathogenesis of the lymphangiomata and cystic hygroma is discussed.

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COMMON INJURIES OF THE KNEE JOINT SUSTAINED IN AUSTRALIAN RULES FOOTBALL.

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Melbourne.

IN the southern States of Australia, at this time of year, almost every youth, or would-be youth, has donned football boots and is attempting to force his way into a football team, in either local grade or professional league football.

There is an extremely high incidence of injuries to the knee joint, and the medical officer of a football club is not given any great guidance by his medical education, or by medical literature, in the management of these injuries. Residual disability following injury to the knee joint has caused the enforced retirement of some of the most talented players. There is probably a higher incidence of residual disability from knee-joint injury than from any other trauma commonly sustained in Australian rules football. The best preventive measures are skill and physical fitness, although, unfortunately, even the most skilful are not immune from injury.

The knee joint is no better than the muscles that cross it. Allowing a player to return to football with any weakness of the quadriceps muscles is inviting serious damage to the knee. The presence of any fluid in the knee, apart from indicating joint damage, causes instability. Under no circumstances should a player with fluid in the knee be allowed to "take the field".

Diagnosis of the Injury.

Probably in no part of surgery does the diagnosis depend so greatly on an accurate history of the incident. The boy should be asked to describe in detail exactly what happened. Ideally he should be examined immediately after injury and an attempt at assessment made.

Most Melbourne and country league teams have a medical officer interested enough in football to attach himself to the team. It is, therefore, in most cases, possible to have an examination of the knee made within minutes of the injury. This should be done in the medical room—that is, isolated from all newspaper reporters, supporters, committee men and well-wishers.

By immediate assessment, we are able (i) often to make a diagnosis that would be obscured by the subsequent effusion, (ii) to prevent the player from aggravating any injury by continuing to play with an injured knee. After any knee injury there is an effusion into the joint which may obscure the diagnosis.

In all cases an X-ray picture is taken.

With any football injury we must aim to restore the player to the condition of a first-class athlete. Everything we do or say to the boy must encourage the fullest cooperation if this object is to be achieved.

The types of injury seen in the knee joint fall into the following four main groups: (i) contusion, (ii) ligament sprain, (iii) ligament tear, (iv) meniscus injury. These injuries may occur in combinations. Ligament injury often is associated with meniscus damage.

Contusion.

Contusion, the least serious, is caused by a direct blow on the tissues about the knee joint. Usually it is caused by a kick. These boys are often first seen at the half or three-quarter time intervals, as the player has not regarded the condition seriously enough to leave the field. Except with a very minor trauma, the subsequent changes are, first, a synovial effusion occurring during the next 12 to 24 hours. This is followed by quadriceps wasting. I have seen the quadriceps waste two inches in a week, when the boy has not been conscientious with his exercises.

On examination there is an area of localized tenderness associated with an area of bruising at the site of the injury. If the knee is examined after there has been delay, there is also an effusion into the knee joint, which obscures the clinical picture to some degree.

The object of our treatment is primarily to prevent the effusion into the knee joint. This is done with a firm pressure dressing, which is placed on the knee the moment the boy leaves the field, and remains on for a minimum of 48 hours. From the time of the injury, he has the most intensive quadriceps exercises. It is the effusion and the quadriceps wasting that will prevent him from making his early return to the football team. The quadriceps exercises should be continued long after the knee injury has subsided and been forgotten. Normally the boy will not be allowed to play football until the quadriceps are normal and there is no fluid in the knee.

During his time of incapacity, he is put into the hands of the physical therapy instructor, who works out the most intensive exercises to keep the player's heart and lungs in their original state of tone. After a knee injury, I have seen players go on to the arena wearing a support of crêpe bandages on their knees. I believe that if a player needs a crêpe bandage, he must be unfit and should not be on the arena. He will run the risk of permanent damage to the knee. No matter how great a star, he will not play as well as the completely fit average player. The only occasion on which a player should be allowed to wear a crêpe bandage is after a minor contusion, when

no replacement is available, and he has been allowed to continue the game.

The average time before returning to full training is in the order of a week to ten days, sometimes more, sometimes less, according to the severity of the contusion.

Ligament Sprain.

Ligament sprain is caused by direct violence, usually by someone falling across the victim's extended leg. By ligament sprain, let us imply partial tearing of one of the ligaments, usually one of the collateral ligaments or the posterior ligament. The player suffers immediate severe pain in the knee. Nearly always he has to be assisted to leave the ground.

On immediate examination, there is pronounced local tenderness over one of the ligaments, usually at the upper or lower end of the ligament. Severe pain is produced when the ligament is forced on to tension by "springing" the joint. There is no joint instability. At this stage there is not yet any effusion into the joint. As in all injuries of the knee, an X-ray picture is taken to exclude any underlying bony damage that would otherwise be undiagnosed. During the next 24 hours, a most tense effusion occurs into the knee joint.

The object of treatment is (i) to prevent this effusion, (ii) to give complete and absolute rest to the ligament until it is firmly healed, (iii) to prevent quadriceps wasting.

A firm pressure bandage is applied, in an attempt to prevent an effusion from forming. If on the following day the knee is tense, the fluid in the knee should be aspirated under a full aseptic operating theatre régime. A plaster back slab is made on which the limb is rested, and this back slab is used until the boy's knee is pain-free. The most intensive quadriceps exercises are commenced on the day after the injury.

For the young active footballer, there is only one way to rest the part completely and absolutely. This is to use plaster and to make the boy walk with crutches. I am convinced that this complete and absolute immobilization of the knee, associated with the most intensive quadriceps drill, can reduce the disability time by approximately 50%. The average time off competitive football is in the vicinity of three to five weeks, depending on the severity of the injury.

While the player is bound up in plaster, he is once again kept fit in the gymnasium by exercises to the remainder of his body. Intensive quadriceps exercises are continued till long after the knee has apparently returned to normal.

Under no circumstances is the boy allowed on the field (i) if there is any tenderness, (ii) if there is any fluid in the joint, (iii) if there is any quadriceps wasting. He would otherwise not acquit himself well and would risk permanent damage.

Ligament Tear.

Ligament tear is caused by direct violence more severe than that which caused ligament sprain. In six years with the one club I have had only four cases of complete ligament tear. There is a history of someone having fallen heavily across the victim's extended knee. In all the cases, the player had to be carried from the ground because of instability of the knee and pain in the knee.

On immediate examination, before the inevitable effusion has occurred, there is pain over the ligament, but very much less severe than the pain associated with sprain. It may be possible to feel a gap in the ligament. There is marked instability in the knee, depending of course, on the particular ligament torn. With lateral or medial ligament tear, the knee joint can be opened up like a book. In cruciate ligament tear, there is marked antero-posterior instability. During the next 24 to 48 hours, a most tense effusion occurs into the knee joint, making the diagnosis difficult at this stage; hence the need for early assessment. In all cases an X-ray picture is taken.

Immediately a firm pressure bandage is placed on the knee, and a strong plaster back slab is used to immobilize the knee. On the following day, if the effusion is tense, it is aspirated. In each of the cases, the limb was immobilized in plaster for a period of six weeks. During this period of immobilization, intensive quadriceps exercises are undertaken. Strangely enough, in each case, the injury happened towards the end of the season, so the decision did not have to be made as to when the boy should return to football. I would be most hesitant to allow a player to return to competitive football in the same season. In none of the cases was operation undertaken.

All the boys with a torn collateral ligament returned to football of no less quality than before the accident. One of the boys had torn, as well as the medial and posterior ligaments of the joint, the cruciate ligaments of the knee joint. His knee joint is now quite adequate for farm work, but is too unstable for him to be allowed to return to football.

Meniscus Injury.

Meniscus injury is one of the commoner injuries associated with Australian rules football. It occurs more frequently than sprain or ligament tear. In my experience, the injury seems more likely to occur either in the first year of play or at the end of a boy's career.

The history is quite typical. By seeing the incident, or having an accurate description of the injury, one can make the diagnosis. The typical injury is of sudden forced rotation with the foot firmly fixed on the ground and the knee partially flexed. The footballer falls to the ground with severe pain in the knee, and is unable to get up. In about 50% of cases the knee joint is locked by a fragment of torn cartilage. The boy says that he has felt something tear within the knee, and often that he has felt something move within the knee joint. The condition is notoriously difficult to diagnose with certainty unless there has been a history of locking.

On examination, the joint may be locked. Tenderness is present over the joint line anterior or posterior to the collateral ligament. A bulge caused by the displaced cartilage may be seen anterior to the collateral ligament if the joint is locked. An X-ray picture is taken.

Our first-aid men are instructed that under no circumstances are they to attempt to manipulate the knee. The player is carried off the ground, and an immediate assessment is made in the medical room. If there is a history of locking, and perhaps more important, a history of unlocking, and an X-ray picture shows no opaque fragment within the joint, one may be sure that the injury is a torn meniscus.

If the knee joint is locked the boy is transported to hospital, where, after X-ray examination, the limb is manipulated under general anæsthesia to unlock the joint. This procedure is followed by the application of firm pressure bandages applied to prevent effusion. A plaster back slab is applied to give complete rest. The boy is given crutches, and forbidden to walk on the injured limb. Perhaps the most important factor in treatment is the commencement of intensive quadriceps exercises.

From the moment of injury the dangers of quadriceps wasting are explained to the player, and he is urged and encouraged to prevent this wasting.

If there has been locking, there is no doubt that the sooner the cartilage is removed, the more likely is the boy to return to full quality football. If the condition is treated early, there is less likelihood of permanent damage to the hyaline cartilage of the joint. When one sees the state of the knee joint in cases of long-standing cartilage derangement, one realizes why the results of surgery are so unpredictable. The long-standing injury untreated makes osteoarthritis inevitable in middle age.

If there is no history of locking, one is more hesitant to urge operation. My principle is to continue immobilization and quadriceps exercises until there is (i) freedom from pain, (ii) no effusion, (iii) no quadriceps wasting.

The boy is then given a trial at normal football. If he breaks down, surgery is undertaken to remove the torn cartilage.

After surgery he is not allowed back into football until there is no fluid and no quadriceps wasting. I believe that it is unwise to return to football in the same season. It is the delay in surgical treatment and the lack of appreciation of the dangers of quadriceps wasting that have made cartilage operation of doubtful repute amongst footballers and football committees.

Conclusion.

The footballer, unlike other members of society, has a fanatical desire to return to full activity at the earliest moment. We must therefore protect him from himself and from the football club committee, and insist on treatment until the knee joint has returned to "normal". "Normal" to this boy means the knee of a champion athlete. Never hesitate to share the responsibility and ask for a second opinion, as the response to treatment after knee injury is often difficult to predict.

Records kept for this particular group over a period of six years have quite convinced me that the unfit star is no match for the average fit player.

Reports of Cases.

SARCOMA OF THE STOMACH OF LYMPHOID ORIGIN: A REPORT OF FIVE CASES.

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SARCOMA of the stomach is a relatively rare tumour; the incidence as reported varies from 1·5% to 3·2% of all malignant gastric tumours. Of these from 40% to 60% are lymphoid in origin, and it is with these that this paper deals. Occasionally the gastric lesion is part of a generalized disease, but we are concerned only with those arising primarily in the stomach.

Although this tumour is relatively rare, it is of interest in that the five-year survival rate is far better than that for carcinoma of the stomach. Snoddy (1952) collected 474 cases reported to that date and gives an overall five-year survival rate of 10·5%, with an operative mortality of 34%, whereas the overall five-year survival for carcinoma of the stomach at that time is given as 1–2%.

Marshall and Meissner (1950) reported a series of 41 cases from 1929 to 1949, of which 32 were lymphoid in origin. Seventeen of these 41 patients survived for five years, giving a 44% survival rate.

Marshall and Adamson (1959) reported 62 cases, of which 11 were classified as Hodgkin's disease. The remaining 51 cases showed a five-year survival rate of 39·2%.

Snoddy's figures are adversely affected, in regard to the other two quoted, by the operative mortality rate of 34%. This figure was compiled from all world figures to that time and is no reflection on the author. The present mortality figure over a series of this size should be no greater than 5%, which would correct his five-year survival to about 40%.

Therefore it is felt that one can now anticipate at least a 30% to 40% five-year survival in gastric sarcomas of lymphoid origin.

The tumour has no clinical features which can definitely differentiate it from a carcinoma before operation. An analysis of the symptomatology as reported in the literature confirms my own findings in this. Epigastric discomfort or pain, anorexia and weight loss are constant findings and their presence serves no purpose in the differential diagnosis.

The gross appearance of the stomach at operation is fairly typical. The gastric wall is occupied by a large, flat mass, often showing shallow ulceration on the mucosal surface. Occasionally the tumour infiltrates beneath the intact mucosa and throws it up into giant rugæ. The cut surface shows great thickening of the gastric wall, which is yellowish-white in colour. The serosa is often intact and shows none of the seeding so often associated with carcinoma. Metastasis to lymph glands occurs in about half the cases. These glands are greatly enlarged, fleshy and usually mobile. Liver metastases are not seen.

The pathology of these tumours is interesting. They take origin in the lymphoid tissue of the submucosa and occasionally in the deepest layers of the mucosa.

The most common mode of spread is by direct extension in the submucosa beneath the intact mucous membrane, which gives the gross appearance of a plaque-like mass. Due to the interference with the blood supply, shallow ulceration of the mucosa may occur. Occasionally the submucosal spread has the effect of raising the mucosa into giant rugæ. Spread may occur directly outwards penetrating the muscle coat and serosa. This is less common. Occasionally the lymphoblasts penetrate directly through the gastric wall, growing rapidly and causing central necrosis as growth outstrips the blood supply. This type may cause acute perforation.

Histologically the majority of tumours are reticulosarcomas with a small percentage of lymphocytic or giant follicle tumours. They are easily recognized under the microscope by the massing of cells and the entire absence of epithelial differentiation.

Five cases of primary lymphoid tumours of the stomach are presented. Three of them are histologically reticulum cell sarcomas and two are lymphosarcomas. The three reticulosarcomas are personal cases. They were collected during the five years from 1955 to 1960, so no five-year survival figures are quoted. Four were from the surgical unit of a large general hospital where, during the same period, 125 carcinomas of the stomach were seen. This represents an incidence of 3·2%. The fifth case was from a smaller hospital, where it was not possible to estimate a figure of incidence. The series comprises two females and three males, varying in age from 42 years to 69 years.

Case I.

The patient was a female, aged 42 years, who presented on December 12, 1955, complaining of twelve months' history of loss of appetite and loss of weight, and epigastric discomfort for six months. Two months prior to her hospital admission she had a sudden attack of severe left-sided abdominal pain lasting two hours. These attacks continued at intervals for two weeks, when she noticed a tender swelling on the left side of her abdomen.

Physical examination revealed a tender, palpable mass on the left side of the epigastrium, attached to the anterior abdominal wall. A full blood count showed a hæmoglobin level of 8·7 grammes per 100 ml. and 10,400 leucocytes per cubic millimetre, of which 60% were neutrophils. A provisional diagnosis of perigastric abscess secondary to perforated ulcer or carcinoma was made and a laparotomy was performed on December 16, 1955. The operative findings were that there was an extensive flat tumour of the distal third of the stomach invading the posterior rectus sheath with an associated perigastric abscess. Fleshy glands were found along the upper border of the pancreas. No liver metastases were present.

A high partial gastrectomy with excision of the posterior rectus sheath was performed as a palliative measure.

She made an uneventful post-operative recovery. The pathological report on the tumour showed it to be a reticulum-cell sarcoma and the tumour extended to the free cut edge of the stomach. The lymphatic glands showed no sign of malignancy. She was referred to another hospital for radiotherapy, which commenced on January 26, 1956. She died on April 3, 1956. The causes of death were (i) cachexia; (ii) gastro-colic fistula; (iii) abdominal wall extension of gastric sarcoma.

Case II.

The patient was a male, aged 50 years, who was admitted to hospital on July 8, 1957, complaining of loss of weight and anorexia for the past three years and vomiting after meals for the past twelve months. He made no complaint of abdominal pain. Physical examination revealed no abnormalities. The barium-meal X-ray examination revealed a large quantity of fasting fluid and the terminal two inches of the stomach was constantly narrowed and deformed and failed to pass peristaltic waves. The appearance suggested stenosis of the terminal portion of the stomach probably due to neoplasm.

Laparotomy was performed on July 22, 1957. The distal portion of the stomach was occupied by a diffusely infiltrating mass. Enlarged glands were present along both curvatures. No liver metastases were present. A partial gastrectomy was performed, but it was felt that the tumour was incompletely removed.

The patient's post-operative course was uneventful. The pathological report showed the tumour to be a reticulum-cell sarcoma which extended to the free cut edge of the stomach. The lymphatic glands were not involved. He was given radiotherapy after operation. He returned to his normal occupation as a labourer and, when last reviewed in 1960, had gained weight and had no symptoms or signs of recurrence.

Case III.

The patient was a woman, aged 49 years. She was admitted to hospital on October 15, 1958, complaining of epigastric pain which had been present for several years. She had had a hæmatemesis four years previously. There had been a few pounds' loss of weight in the past few months. Her hæmoglobin value on admission to hospital was 8 grammes per 100 ml. Gastroscopy was attempted, but failed. A barium-meal X-ray examination on October 22, 1958, showed an ulcer high on the greater curvature with some enlargement of the surrounding gastric folds. The ulcer appeared simple.

On November 11, 1958, laparotomy was performed. The ulcer was locally excised and a partial gastrectomy was performed below the ulcerated area. It was noticed that the stomach wall around the ulcer was indurated and some large, soft lymphatic glands were present along the greater curvature. The histological preparations showed a lymphosarcoma with a tendency to follicle formation. The tumour was incompletely removed. The lymphatic glands were not involved. Post-operative radiotherapy was given. She is at present well, and has no obvious signs of recurrence either clinically or radiologically.

Case IV.

The patient was a male, aged 65 years, who was admitted to hospital on December 28, 1958, for treatment of a peptic ulcer of some years' duration. Just prior to admission he had had a hæmatemesis. His hæmoglobin value on admission was 5·5 grammes per 100 ml. A barium-meal X-ray examination performed three weeks after admission showed a large, shallow ulcer at the distal end of the lesser curvature. The appearance suggested gastric carcinoma. On February 3, 1959, a laparotomy and partial gastrectomy were performed. No glands or liver metastases were present. The macroscopic appearance of the lesion itself suggested a simple ulcer. The histological preparation showed a lymphosarcoma.

The patient received post-operative X-ray therapy, and is now well and shows no evidence of recurrence or metastasis.

Case V.

The patient was a male, aged 69 years, who was admitted to hospital on April 9, 1960, suffering from an acute perforation of a gastric ulcer which was oversewn. The surgeon who performed the operation noted some induration of the stomach wall around the perforation, which was 1·5 cm. in diameter and was situated on the anterior wall of the lesser curvature. No biopsy was performed.

He had complained of indigestion for six months prior to the perforation and a barium-meal X-ray examination in January, 1960, revealed no lesion in the stomach or duodenum.

Shortly after his discharge from hospital, he commenced to pass dark stools and a further barium-meal study showed some distortion of the distal portion of the stomach; this was thought to be due to the recent surgery. He continued to complain of weakness, epigastric pain and loss of weight. On admission to hospital on July 30, 1960, his hæmoglobin value was 7·6 grammes per 100 ml. A further barium-meal study was done on August 4, 1960. This showed much irregularity of the distal half of the stomach, with a large associated filling defect. The appearances were typical of a malignant neoplasm.

On August 10, 1960, a laparotomy was performed. The distal half of the stomach was infiltrated and thickened, and large, fleshy glands were present along both curvatures. No liver secondaries were present and there was no peritoneal seeding.

A high partial gastrectomy was performed, but it was not thought that the tumour was completely excised. The macroscopic appearance was that of a lymphoid sarcoma. Microscopy confirmed that the tumour was a reticulum-cell sarcoma. The lymphatic glands were not involved. The patient was given post-operative radiotherapy, and is now well and gaining weight.

Discussion.

These clinical histories have been given in some detail, as they each present some interesting features, which are summarized in Table I.

An analysis of the symptoms shows that weight loss is common to all five cases, and epigastric pain and anorexia to four out of the five. This agrees with Marshall and Adamson (1959), Marshall and Meissner (1950), and Snoddy's (1951) series, as being the cardinal symptoms of which the patient complains. However, three patients out of five had hæmatemeses and/or melæna, which they claim are very rare symptoms. Two out of five lesions perforated—an event to which I can find no reference in the clinical literature, and Stout (1957) in describing the pathology, refers to it only as a possibility.

Anæmia, as a rule, does not occur in the absence of hæmatemesis or melæna. This we would expect as the lesion is often non-ulcerative.

There are no distinguishing features about this tumour which will allow us to make a definite pre-operative diagnosis. The symptomatology is exactly similar to that of carcinoma of the stomach. The clinical findings are unremarkable apart from the absence of anæmia in those cases of sarcoma which show no evidence of frank hæmorrhage. In carcinoma anæmia is common in the absence of frank hæmorrhage. However, I do not wish to put this forward as a method of differentiating between the two lesions. The barium-meal study is not helpful, as three of the four cases reported in which X-rays were taken were diagnosed only as neoplasms, and one as a simple ulcer. This corresponds with other authors' findings.

At operation suspicion of the nature of the neoplasm may be aroused. The tumour is flat and extensive. The lymphatic glands are enlarged, pink, discrete and rather elastic in consistency. The liver does not show metastases and peritoneal seeding even locally is not seen. The cut surface of the tumour is yellowish-white, and the mucosa is either intact or shows shallow ulceration, and giant rugæ may be present. However, in spite of these findings, as Bockus (1943) stated: "Nothing short of histologic examination can determine the diagnosis of gastric sarcoma."

Conclusions.

Primary lymphoid sarcoma may be expected to be found in from 1·5% to 3·2% of all gastric neoplasms encountered. Its prognosis is much better than that of gastric carcinoma.

TABLE I.

Features of Five Cases of Sarcoma of the Stomach of Lymphoid Origin.

Case.	Epigastric Pain.	Anorexia.	Weight Loss.	Hæmatemesis or Melæna.	Anæmia.	Perforation.	Barium Meal Diagnosis.	Tumour Type.	Glands.	Survival.
I	Yes.	Yes.	Yes.	No.	No.	Yes.	Not done.	Reticulum cell sarcoma.	No.	Dead (4 months).
II	No.	Yes.	Yes.	No.	No.	No.	Malignant neoplasm.	Reticulum cell sarcoma.	No.	Alive and well (40 months).
III	Yes.	No.	Yes.	Yes.	Yes.	No.	Simple ulcer.	Lymphosarcoma.	No.	Alive and well (23 months).
IV	Yes.	Yes.	Yes.	Yes.	Yes.	No.	Carcinoma.	Lymphosarcoma.	No.	Alive and well (20 months).
V	Yes.	Yes.	Yes.	Yes.	Yes.	Yes.	Malignant neoplasm.	Reticulum cell sarcoma.	No.	Alive and well (2 months).

It is impossible to diagnose the condition with certainty in the absence of histological preparations, and therefore, all patients with gastric neoplasms should have a laparotomy and at least a biopsy, whether the condition be deemed inoperable or not. All patients with ruptured gastric ulcer should have an adequate biopsy taken from the ulcer edge.

Surgery, followed by radiotherapy to the stomach stump and the lymphatic drainage area, is the treatment of choice.

Summary.

Five cases of lymphoid sarcoma of the stomach are presented, with a brief account of the pathology of this condition.

An analysis of the symptomatology is made with reference to other reports, and the impossibility of making a correct diagnosis in the absence of biopsy is stressed.

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AMAUROTIC FAMILY IDIOCY: A REPORT OF A FAMILY SUFFERING FROM THE JUVENILE FORM OF THIS DISORDER (BATTEN'S DISEASE).

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AND
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HISTORICALLY, amaurotic family idiocy was first described in 1881 by Warren Tay, an ophthalmologist, who made observations on the eye grounds of Jewish children. Six years later, in 1887, Sachs made further detailed observations on this condition, hence the disease became known as Tay-Sachs disease. Batten (1903) was the first to recognize that the disease is not exclusive to infancy but can, and indeed does, occur at a later age. Vogt (1906) and Spielmeyer (1906 and 1907) similarly described cases which correspond to Tay-Sachs disease, the essential differences being that in the latter condition the onset is during the first year of life, the disease is limited largely to Jewish children and a cherry-red spot is present in the eye grounds. The condition described by Batten, Vogt and Spielmeyer differed in that the onset was later, the disease occurred in Gentiles and the eye fields showed retinitis pigmentosa. This disease is currently referred to as the juvenile form of Tay-Sachs disease, or Batten's disease or Vogt-Spielmeyer's disease. Whatever name is given to it, the juvenile form of amaurotic family idiocy is now an established disease entity.

In spite of the detailed and clear classification of this disease, Schob (1912) stressed the fact that the clinical diagnosis of the juvenile type is difficult, particularly so when cases occur sporadically. The same view was held by Spielmeyer (1923), Higier (1926) and others. All authors agree that this disorder is rarely seen.

However, Sjögren (1931), in his description of 59 cases of the juvenile form of amaurotic idiocy, was able to show that the clinical picture and course were highly uniform; this usually allows for a correct clinical diagnosis even when the disease occurs sporadically — that is, when only one member of the family is afflicted.

Ætiology.

It has long been recognized that there is a marked hereditary tendency to this disease and instances have been published of its appearance in several generations of a family. Sjögren (1931) suggested that the disease is probably an enzyme defect, analogous to that in phenylketonuria, and that, as in the latter condition, it is due to a single recessive-gene abnormality. The disease is distributed equally between males and females.

Pathology.

To the naked eye, the brain appears hard, and there is widening of the Sylvian fissures, with marked atrophy of frontal convolutions. The most noticeable microscopic change is an accumulation of lipoid substance in the cortical neurons with a consequent characteristic ballooning of the cells and swelling of the axons and dendrons. The nucleus is displaced towards the apex of the cell and there are rarely any healthy Nissl granules. These changes are usually most marked in the cortex; but are also present in the basal ganglia and to a lesser extent in the cerebellum, pons, cord and sympathetic nervous system. With them there is usually a degeneration of myelinated fibres of the white matter and a considerable proliferation of neuroglia; but inflammatory changes in the vessels and meninges are not present.

Clinical Records.

The family consisted of four children — one girl who died of this disease, two boys who are afflicted and one

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boy who is thus far well. There is nothing of significance in the past histories of the parents and antecedents; there is no suggestion of consanguinity.

First Male Child.

The patient was admitted to the Admission Centre, Darlinghurst, at the age of 15 years, with a history, commencing at the age of six years and 10 months, of increasing blindness, progressive dementia, convulsions and progressive, generalized weakness and wasting. He had had a normal birth and had weighed eight and one-quarter pounds. His development, both mental and physical, was quite normal until the age of six years and 10 months, when backwardness at his school work was noticed; at this stage he was found to be partially blind. In the next few years his vision, his school work and his mental state steadily deteriorated — so much so that his attendance at school was discontinued. He had his first major epileptic convulsion at the age of 12 years, and these convulsions gradually increased in frequency; at the time of his admission he averaged one fit per month. His muscles became so wasted and weak that he was bedridden and he recently had developed incontinence of urine. At the time of his admission to hospital, this dark-haired boy of 15 years was almost completely demented. He would answer only simple questions in a flat, indistinct and expressionless voice, and obey only simple instructions. He was generally cooperative with the staff, but he had to be hand fed, and from time to time would give an involuntary shout. Weakness and wasting were present in all his muscles, with reduced tone. His tendon responses were poor; the abdominal and cremasteric reflexes were present and the plantar responses were flexor. Apart from a bilateral, coarse nystagmus on forward vision, the cerebellar function appeared to be within normal limits. The fundi showed typical bilateral retinitis pigmentosa involving both eyes. He had complete loss of vision in both eyes. The boy's condition continued to deteriorate, both physically and mentally, and he was admitted to an institution for mental defectives. The electroencephalogram reveals generalized, slow activity at 4 to 7 cycles per second, and the record shows runs of moderately high-voltage slow activity at 2 to 4 cycles per second occurring bilaterally in the parietal and occipital regions, with some wave-and-spike complexes at the same frequency.

Second Male Child.

The history and general progress of the second son of the family is essentially the same. His condition also deteriorated to such a degree that his admission to an institution became necessary. The electroencephalogram shows generalized, slow activity at 4 to 7 cycles per second without focal or lateralizing features. There are posterior slow rhythms of moderately high voltage in the parietal and occipital regions bilaterally at 2 to 4 cycles per second. There is also paroxysmal activity characterized by high-voltage (3 cycles per second) wave-and-spike complexes. There are no focal or lateralizing features.

The appearances of both these tracings are very characteristic of a tendency to epilepsy, and in fact the first boy's record shows 3 cycles per second wave-and-spike complexes which are very characteristic of true *petit mal*. Although there are occasional multiple spikes on a slow wave, the appearances are not sufficiently in accord with the changes described as characteristic of cerebral lipidosis to permit a statement as to any certain relationship, although it may well be that they are directly the result of cerebral lipidosis. The other possibility is that there is an independently inherited constitutional dysrhythmia, with a liability to epilepsy which has become manifest at this time. We would incline to the view that this latter possibility is less likely. However, the electroencephalographic appearances do not permit a definite distinction to be made.

Female Child.

The daughter of the family was a patient in an institution and died at the age of 16 years from this disease. No electroencephalographic records or autopsy reports are available.

Third Male Child.

The third son, aged 10 years, is a bright lad, with no signs of any physical or mental abnormality.

Discussion.

It has been stated earlier that most authors agree that the juvenile form of amaurotic family idiocy is diagnosed clinically with difficulty. It is hard to understand why this should be so if a careful clinical study is made of each case. The vast majority of cases present a very similar clinical picture, and indeed Sjögren (1931) spoke of a "photographic similarity" in all cases.

The clinical course of the disease may be divided into five stages, but before these are discussed it may be said that there is a uniform finding in the eye fields, as well as characteristic abnormalities in posture and gait and a marked mental deterioration.

The first stage of this malady is ushered in by visual disturbances leading to total blindness within one to two years. Ophthalmoscopically there is retinitis pigmentosa and optic atrophy. The onset is usually between the ages of five and eight years.

The second stage is characterized by the onset of epileptic fits in the form of *grand mal* attacks. On the average these occur at about 10 years of age. At about the same time mental changes in the form of lack of emotional control, irritability, hyperkinesis, apathy and even imbecility make their appearance. Speech also shows alterations, such as stammering, explosive articulation and echolalia.

In the third stage marked and definite mental deterioration becomes obvious. Attention, memory and judgement are impaired, and the child quickly forgets what he has learned. The personality changes are even more severe. The child is entirely disinterested in the environment and is apathetic and irritable. The face is rigid and devoid of expression, but spasmodic laughing and weeping occur. Speech is monotonous and articulation is indistinct. The content of the speech is stereotyped and shows a strong tendency to perseveration. Poverty of words and ideas becomes striking. In this stage significant neurological symptoms make their appearance; all movements become slow; typical rigidity and abnormal postures are present. A characteristic disturbance of this stage is the peculiar gait, the *marche à petit gras*, a dragging gait with short, slow steps. The knees are flexed and the patient does not lift his feet, but walks with the whole sole on the floor. The arms are not swung in walking. In some cases tremors both of rest and of intention are present and the picture is that of a Parkinsonian syndrome. The tendon and superficial reflexes are usually normal or reduced. The plantar responses are usually, but not necessarily, extensor and there may be a Romberg sign. Examination of the cranial nerves often reveals nystagmus and strabismus. Sjögren stressed the fact that hearing was normal in almost all cases. Vegetative disturbances are sometimes present in the form of acrocyanosis of both hands and feet.

In the fourth stage the mental defect has reached the degree of idiocy. The patient is apathetic, fails to notice his environment and hardly ever speaks; when he does his speech is limited to a few inarticulate sounds. He does not react to external stimuli; he becomes almost completely helpless. The apathy may at times be interrupted by prolonged screaming, crying and restlessness. Neurological and vegetative disturbances become more severe and the gait regresses rapidly, the patient walking only with support. The musculature now begins to waste, but still shows a good deal of strength.

In the final or fifth stage of the disease the patient is totally amented and paralytic. He is now totally helpless and incontinent, and speech is almost completely absent. The musculature is grossly atrophied and partial reaction of degeneration is present. The plantar responses are extensor and the tendon jerks are increased. Acrocyanosis is marked. Epileptic fits are frequent and the patient usually dies in status epilepticus or from intercurrent infection. Sjögren found the average age of death to be

about 18 years and the course of the disease from 10 to 15 years.

It will be seen that Batten's disease is met more often than is usually appreciated. If a careful and detailed history is taken diagnosis should present no difficulty.

When one is considering differential diagnosis the following conditions should be remembered. (i) Juvenile general paralysis of the insane, when accompanied by optic atrophy, may sometimes produce a clinical picture which is similar in certain respects to that of Batten's disease. However, in addition to the positive serological findings and the presence of other syphilitic stigmata such as osteitis, saddle nose, interstitial keratitis and particularly disturbances in hearing, the disease can be differentiated by the course and development of the amaurosis. Furthermore, in Batten's disease one sees bilateral retinitis pigmentosa leading to total blindness, while in juvenile general paralysis of the insane this is seldom seen and usually does not produce such pronounced loss of vision. (ii) Cerebral sclerosis, described by Scholz, is characterized by a rapid course, the absence of degenerative retinal changes and deafness. (iii) There are a few rare disorders which may sometimes produce a clinical picture similar to that of Batten's disease. Among these are the cerebral sclerosis of Krabbe, the cerebral sclerosis of Pelizaeus and Merzbacher, Friedreich's ataxia with spasticity, and acquired hydrocephalus of various origins. All these can be easily differentiated from Batten's disease when consideration is given to the latter's typical onset, course and development with the characteristic stages and symptoms, and when it is remembered that in all cases of Batten's disease there in such constancy, that, with Sjögren, one can speak of a "photographic similarity" in the great majority of cases, the diagnosis of Batten's disease should present no real difficulty.

Summary.

A family suffering from Batten's disease is presented. Diagnosis and differential diagnosis are discussed.

Acknowledgements.

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Reviews.

Anaerobic Bacteriology in Clinical Medicine. By A. Trevor Willis, Ph.D. (Leeds), M.B., B.S. (Melb.); 1960. London: Butterworth & Co. (Publishers) Ltd. 8½" × 5½", pp. 180. Price: 43s. 6d.

THIS admirable little book attempts "to provide the reader with concise information on anaerobic technique and on the determination and evaluation of the properties of the clinically important anaerobic bacteria". In this task the author has been eminently successful.

The first chapter on methods of growing anaerobes sets out clearly the different techniques that may be used in the laboratory to achieve anaerobiasis. The second describes simply but adequately the preparation of suitable media. The third deals with the identification of isolated organisms. These chapters form an excellent practical guide for clinical pathologists who are inexperienced in this field.

The distinguishing characteristics of the different species of anaerobes of clinical importance are discussed in chapter four. The clostridia occupy 30 pages, whilst the remainder—anaerobic cocci, fusiform bacilli and actinomycetes—have 12 pages between them. This emphasis on the spore-bearers could give an incorrect impression of the relative frequency of the different types of anaerobic infections in peace-time medicine, but it no doubt reflects a special interest understandable in one working with Professor Oakley, whose long series of brilliant studies of this group have made him the expert in the genus.

The next chapter, which includes advice on treatment, is also somewhat uneven. In the section on management of tetanus, for example, over a page is given to the therapeutic use of antitoxin, whilst the prognostically vital problem of control of spasms is dismissed with a brief "muscular relaxants and sedatives are given".

However, these are minor criticisms of an apparent imbalance which is easily explained by the genesis of the book. As the preface states quite frankly, the original resolve was to produce a book on anaerobic technique. As the manuscript grew "a little was added here and a little there"; but even in its final form there is no suggestion that it is a complete manual of both diagnosis and treatment of all varieties of anaerobic infections. As a reliable and encouraging guide to a hesitant clinical pathologist reluctantly forced to embark on some unwelcome anaerobic bacteriology, it is first rate. Even to one free of such responsibility it is a pleasure to read. Trevor Willis's enviable ability to write simply and clearly may, or may not, have a genetic basis; but the author of the classical texts on tumour pathology will not be ashamed of his son's first book.

The Organization of Cells and Other Organisms. By Laurence Picken; 1960. Oxford: The Clarendon Press. 9¼" × 6", pp. 668, with many illustrations. Price: 121s.

As the author states in the preface, this book is a compilation for post-graduate students and research workers. His intention is to attempt a synthetic picture of the organization of cells in terms of macromolecular structure and texture. The "other organisms" in the title are viruses and bacteria, for it has not yet been proven that viruses are living organisms, nor have bacteria been proved to have true mitoses, a nuclear membrane or certain other attributes of true cells.

There are chapters on the organization of cells, of viruses and of certain schizomycetes, following which other chapters deal in detail with the organization of the nucleus, the cytoplasm, individual components of the cytoplasm and cell surfaces.

There is a chapter devoted to the effect of cells upon their environment, as in the formation of ground substance, fibrogenesis and the formation of membranes. The final chapter discusses the cellular qualities of multicellular organisms.

It is not the fashion for scientists these days to record the concepts from which their experimental procedures

have originated; and now that biological investigation is being reduced to the molecular level, it is becoming increasingly difficult for the casual reader to understand the significance of what he reads. Consequently a book such as this is a pressing need. It gives the general background of contemporary biological research in a readily accessible form, which should be most useful to anyone interested in genetics, biochemistry or radiobiology, not to mention immunology, bacteriology and general cytology.

Community as Doctor: New Perspectives on a Therapeutic Community. By R. N. Rapoport with an introduction by M. Jones, C.B.E., M.D., M.R.C.P.(Edin.), D.P.M.; 1960. London: Tavistock Publications; Springfield, Illinois: Charles C. Thomas. 9½" × 6¼", pp. 332. Price: 62s.

IT is nine years since the publication of Maxwell Jones' "Social Psychiatry", wherein the Social Rehabilitation Unit at Belmont Hospital in England was described. This unit, the first "therapeutic community", was a pioneer in the field of therapeutic social psychiatry, and has highlighted the vital rôle of patients' social relationships in psychiatric treatment. The therapeutic community takes *milieu* therapy as its focus of treatment. By the exposure of the patients to group psychotherapy, work groups, patients' clubs and socials in a constant social interaction process, changes in adaptation and in internal emotional equilibrium occur. With a staff of social scientists, the senior author has clarified many of the implicit assumptions and actual reactions in the unit. He points to the importance of distinguishing "treatment" aimed at intrapsychic change from "rehabilitation" with its emphasis on successful return to outside social networks, and to the need to develop specific policies concerning stages of treatment and differential handling of individual patients.

His hypothesis of "oscillation" in the social organization of the unit, whereby the emotional climate of patients and staff changes in a cyclical manner, is one of importance in explaining difficulties met in the initiation and maintenance of such treatment centres.

The author examines the problem of the psychiatrist's expanding sphere of responsibility. This is traditionally only to the patient, but is now spreading to the treatment of whole families. The Social Rehabilitation Unit has not yet adopted consistent policies in this regard, and a conceptual framework for the analysis of this problem is presented.

Finally the author elaborates a series of postulates based on observation in the unit coupled with the findings of other workers. These are aimed at deriving general principles for the development of therapeutic *milieux* elsewhere. They relate to the formation of a treatment ideology, the organization of staff rôles, the organization of patient activities, the involvement of individuals outside the hospital and the conceptualization of treatment and rehabilitation.

As a critical examination of a particular therapeutic community, this book will be of most interest to psychiatrists, social workers and those involved in modern administrative psychiatry.

First Aid in the Factory. By Lord Taylor, B.Sc., M.D., F.R.C.P.; 1960. London, New York, Toronto, Melbourne: Longmans, Green and Co. Ltd. 8½" × 6", pp. 140 with illustrations. Price: 9s. 6d. (English).

As is stated in the foreword, factory first aid differs from conventional first aid in many respects, not least because the first-aid worker in industry often has to accept full responsibility for the initial treatment of a large number of illnesses and injuries. After investigation, it was found that the existing teaching of first aid bore little relation to the industrial first aider's actual needs, and this book is the result; it goes a very long way towards providing this instruction.

A great deal of the treatment given at an industrial ambulance room consists of the dressing and redressing of comparatively trivial wounds, and the importance of prompt and skilled treatment for these injuries cannot be over-emphasized if disability, suffering and loss of working time are to be avoided. One welcomes the advocacy of the use of sterilized individual dressings, the description of what a first-aid box should and should not contain, and the necessity for the provision of sterilized absorbent cotton-wool and individual sterilized *tulle gras* dressings.

The general principles for dressing and redressing wounds are described, the use of tissue-damaging antiseptics is condemned, and the mechanical cleansing under a running tap of minor wounds is advocated. Whilst the "no-touch" method of treating these wounds is advised, it is surprising that the use of dressing forceps is not mentioned, nor is there any mention of a sterilizer in the ambulance room. As the work of a factory ambulance officer necessitates the dressing and redressing of wounds already infected, and of boils and infected skin lesions as well as of "clean" wounds, the use of a sterilizer for the proper cleaning of kidney dishes, dressing forceps, etc., between dressings, is very necessary, and the statement that "the gallipot, kidney dish, tumbler and eye bath should always be washed thoroughly with soap and hot water and dried on a clean towel" does not reach the standard which can easily be attained by a well-trained ambulance-room attendant.

The use of the individual sterilized pad and bandage in the control of hæmorrhage is discussed.

In the discussion on shock and its treatment, mention is made of the use in Great Britain of morphine by first aiders in coal mines, and by industrial nurses working on the docks. Many will not agree with this practice.

The first-aid treatment of such things as chemical injuries and poisons and chemical burns, and descriptions of the various types of respiratory protection and the different gases and dusts to which the industrial worker may be exposed, furnish valuable information to first aiders on subjects which are only briefly mentioned, or not mentioned at all, in the standard first-aid course.

A fuller description of the mouth-to-mouth method of artificial respiration would have been preferred to the full account, with illustrations, of the various rocking methods of resuscitation which is given.

Instruction in the transport and moving of injured persons is well discussed, and some elementary advice on the care of minor aches and pains is provided.

Particularly helpful is the advice on planning a course to teach industrial first aid, and on the type of examination which should be given at its conclusion, the practical nature of the problems which the industrial first aider will encounter being emphasized.

This is a very useful book, and should be in the hands of all ambulance attendants in industry and of those doctors responsible for their instruction.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Advances in Thyroid Research: Transactions of the Fourth International Goitre Conference", edited by Rosalind Pitt-Rivers, F.R.S.; 1961. Oxford, London, New York, Paris: Pergamon Press. 9" × 6", pp. 538, with illustrations. Price: £6 6s. net (English).

"Handicapped Children", by J. D. Kershaw, M.D., M.R.C.S., M.R.C.P., D.P.H.; 1961. London: William Heinemann, Medical Books Ltd. 8½" × 5½", pp. 228. Price: 21s. net (English).

"Risa Encephalography and Conventional Neuroradiologic Methods: A Comparative Study", by Giovanni Di Chiro; 1961. Stockholm: Acta Radiologica. 9¾" × 7", pp. 102, with illustrations. Price: Sw.Kr. 35.

"Contrast Examination of the Cardiovascular System During Increased Intrabronchial Pressure", by Björn Nordenström; 1960. Stockholm: Acta Radiologica. 10" × 7¼", pp. 110, with illustrations. Price: Sw.Kr. 30.

"Vaso-Seminal Vesiculography in Hypertrophy and Carcinoma of the Prostate with Special Reference to the Ejaculatory Ducts: A Clinical and Experimental Roentgenological Study", by G. W. Vestby; 1960. Stockholm: Acta Radiologica. 10" × 7¼", pp. 194, with illustrations. Price: Sw.Kr. 35.

"The Isometric Relaxation Phase of the Left Ventricle: An Electrokymographic Study", by Osborne Bartley; 1960. Stockholm: Acta Radiologica. 9¾" × 7½", pp. 116, with illustrations. Price: Sw.Kr. 35.

"The Mitotic and Radioprotective Effect of Cysteine and Lysine in Rat", by Lars R. Holsti; 1960. Stockholm: Acta Radiologica. 10" × 7", pp. 100, with illustrations. Price: Sw.Kr. 30.

"Mammary Carcinoma: The Biologic Character of Mammary Carcinoma Studied in 517 Cases by a New Form of Malignancy Grading", by K. A. Hultborn and Bo Törnberg; 1960. Stockholm: Acta Radiologica. 9¾" × 7¼", pp. 144, with illustrations. Price: Sw.Kr. 35.

The Medical Journal of Australia

SATURDAY, SEPTEMBER 16, 1961.

FLUORIDATION OF PUBLIC WATER SUPPLIES.

SINCE we last discussed the question in these columns three and a half years ago,[1] the tide appears to have been flowing fairly steadily in favour of fluoridation of water supplies. Whatever the statistical weakness of the trials which have been carried out, the cumulative weight of evidence in support of fluoridation has won very wide support among those professionally concerned in public health matters, and nothing has happened to justify the warnings of the alarmists about the dire consequences which might follow the introduction of fluoridation. In these circumstances, opposition to fluoridation on the grounds of interference with the liberty of the subject has been a little hard to maintain.

It is true that P. R. N. Sutton has published a trenchant criticism[2] of the statistical methods employed in some of the trials whose results have been most widely quoted in support of the case for fluoridation, but though Sutton was able to show that the statistical lay-out of these trials left a good deal to be desired, and that the statistical results did not support the conclusions to the extent claimed, the fact still remained that experience of fluoridation in an increasingly wide variety of circumstances has been uniformly favourable. Sutton's book is very fairly discussed, along with other matters, in a survey of the present position of fluoridation published in *The Lancet* last year,[3] and the author of this survey concludes with the remark:

> After studying even a small part of the mass of data in the literature of fluoridation, one is tempted to agree with the anonymous writer who said, "the fact that these results are not statistically significant only confirms our view that it is clinical judgement that counts, and in no way invalidates our findings".

However, in general, fluoridation continues to gain ground. The latest available estimate from America is that about 2000 communities in the United States, representing some 38·5 million people, now have artificially fluoridated water supplies. (A further seven million people drink water whose natural fluoride content is equal to, or, frequently, in excess of, recommended levels.) In a considerable number of other countries fluoridation is officially approved, though its introduction in specific localities is frequently hampered by the opposition of vociferous minorities. The position in Australia, as usual, varies from State to State. In New South Wales, permissive legislation is on the Statute Book, and the *Fluoridation of Public Water Supplies Act*, 1957, lays down in elaborate detail how fluoridation is to be done and the standards of accuracy which must be maintained; the Minister for Health has recently reaffirmed his Department's support of fluoridation, Goulburn and Orange are on the point of introducing fluoridation of their water supplies, Yass has been doing so for a number of years, and plans are being prepared for this at Tamworth, where it is intended to carry out a longitudinal survey[4] to obtain factual data on the effects of fluoridation under local conditions. Tasmania is the only other State which has permissive legislation on the subject; a pilot fluoridation scheme has been in operation at Beaconsfield for several years, and it has been announced that Launceston will begin fluoridating its water supply next summer.[5]

At this juncture, publication of a report from the Province of Ontario by a "committee appointed to enquire into and report upon the fluoridation of municipal water supplies" is very apposite. This committee, after almost two years of study and public hearings, has presented an excellently documented report which contains 12 chapters devoted to various aspects of fluoridation. In general, this report reexamines the evidence for and against fluoridation, and the findings are a restatement and confirmation of the advantages of fluoridation claimed by earlier investigators. The report is published by the Government of Ontario, but its findings and recommendations are conveniently summarized in a recent issue of the *Canadian Journal of Public Health*.[6] Some of the more important conclusions of this report are as follows:

1. Dental caries in Ontario is a serious public health problem, and its treatment is beyond the resources of the dental profession.

2. Proper nutrition is a factor in reducing caries but the Committee expresses concern at the inadequacy of "overall nutrition in Ontario".

3. Reduction in caries is a problem of prevention rather than treatment.

4. The presence of fluoride, either natural or added, in public drinking water supplies in concentrations of approximately one part per million "strikingly reduces the incidence of dental caries when such water is consumed during the period of tooth development and . . . the caries reducing effect extends into adult life".

5. The long-term ingestion of fluoride in the recommended amount "over a wide range of water intake is not harmful to body health" and "no fluorosis of esthetic significance is specifically associated with it".

6. The cost of fluoridating a public water supply is very reasonable when compared to the health benefit it confers. (The figure quoted is 10 cents per inhabitant per year.)

[1] MED. J. AUST., 1958, 1:149 (February 1).

[2] "Fluoridation: Errors and Omissions in Experimental Trials". Melbourne: Melbourne University Press; London: Cambridge University Press, 1959.

[3] *Lancet*, 1960, 1:590 (March 12).

[4] This is being planned by the Department of Preventive Dentistry and the Institute of Dental Research in the Faculty of Dentistry of the University of Sydney.

[5] *Sydney Morning Herald*, August 16, 1961.

[6] *Canad. J. pub. Hlth*, 1961, 52:165 (April).

7. The fluoridation of public water supplies is not a "denial of any fundamental or basic civil right or liberty".

Perhaps the most interesting of the Ontario Committee's recommendations is that legislation should be enacted empowering municipalities to fluoridate their water supplies, and that such legislation should authorize municipalities to introduce fluoridation by by-law without the necessity of a referendum. The committee considered that fluoridation has no relation to other issues (e.g., Sunday sport, hotel hours) which are commonly decided by local referendum, and is essentially a question of scientific fact. The procedure suggested is the same as that at present followed when it is decided to chlorinate a public water supply. Further, a Bill to implement the recommendations of the Committee has already been passed by the Ontario legislature. This bill grants authority to municipalities to provide fluoridation without the holding of any referendum. (It provides also that, on a petition signed by 10% of the citizens, a referendum may be held.) In discussing this aspect of the matter the *Canadian Journal of Public Health* aptly remarks: "Experience has shown that a small minority opposed to fluoridation is able to confuse the public making it impossible for them to express an intelligent opinion on a technical procedure."

If we accept the verdict of what appears to be an overwhelming majority of those who have given the question well-informed consideration, that fluoridation of water supply has a very marked beneficial effect on the incidence of dental caries, and that fluoridation to the recommended degree has no possible ill effects, two other questions remain to be considered.

The first is whether fluoridation can be accurately maintained at the right level. The consensus of opinion of those technically responsible for the treatment of water supplies is plainly that this presents no serious difficulty. This question is dealt with in exhaustive detail in a report on "Water Fluoridation Practices in Major Cities of the United States" prepared by the Research Division of the College of Engineering of New York University, for the New York State Department of Health.[7] In this connexion, while water engineers state that the fluoride content can be maintained within 5% of the desired level (that is, to within 0·05 p.p.m.), it may be pointed out that the safe margin of error is in fact extremely wide. Communities have been described whose natural water supply contains as much as 13·7 p.p.m. of fluoride, and quite a number are known with a natural water supply containing 4 to 6 p.p.m. of fluoride. The only demonstrable ill effect is the mottling of teeth which occurs when fluoride is present in high concentrations. The question of tooth mottling (fluorosis) is discussed in some detail in *The Lancet*,[8] where it is stated that a concentration of 1 p.p.m. can cause very mild mottling in about 10% of those exposed, but that this can be detected by expert examination only. Fluorosis produced at levels between 1·5 and 2·0 p.p.m. is still mild and is inconspicuous. (Incidentally, the pigmentation which appears in severe mottling is not directly due to the fluoride ion, but is caused by the absorption of strongly coloured ions such as those of iron and manganese.) Fluoride levels in the neighbourhood of 6 p.p.m. are necessary before mottling becomes severe and disfiguring. It is an interesting fact that of communities whose natural water supplies contain such a high concentration of fluoride that it results in a substantial incidence of dental fluorosis, only one is known which has considered it worth while to instal plant to reduce the fluoride content of the water supply to the recommended level, though it is understood that this presents no difficulty.

The other remaining question is whether fluoridation should be opposed as an infringement of the liberty of the subject. The Ontario Committee have expressed themselves as of "the firm opinion that the fluoridation of municipal water supplies by the authority of appropriate legislation would not be a denial of any fundamental or basic civil right or liberty which the Legislature of Ontario should protect and preserve". They also comment: "The fact that municipal water is fluoridated in no way prevents the exercise of religious liberty as commonly recognized." In fact, other substances have long been added to public water supplies. Professor A. B. Macgregor[8] of Birmingham states: "It is perhaps not realized that the water we drink has a large number of chemicals added to it, in the purification process, including in many instances both chloridating agents and copper salts—both poisonous in high concentration. There is no such thing, therefore, as 'pure' water obtainable from the waterworks, and after conversation with water engineers I believe I am correct in stating that at least 12 chemical compounds are already added to the water." Many other examples of government interference by regulation are accepted as a matter of course. Pasteurization of milk is a good example. This aroused quite strong opposition from some quarters when it was first introduced, but now passes completely unnoticed. This is not intended to imply that such interference should be accepted uncritically, but a good deal of regulation by the government is inevitable in the interests of the health of the community.

An article on fluoridation of water supplies is perhaps incomplete without a glance at the question of the need for fluoridation, and at alternative means of supplying fluorine. The incidence of dental caries in Australia is high, as in so many modern civilized communities, and the dental hygiene of some sections of the community is extremely bad. There is no question, therefore, but that this is a serious public health problem about which the medical profession cannot remain indifferent. It is true that this position could largely be altered if there was a revolutionary change in dietary habits in the right direction, but we know perfectly well this is not in the least likely to happen. On the evidence from many quarters, fluoridation of water supplies would appear to be an easy short cut to a very substantial lowering of the incidence of dental caries. The questions whether the claims of the supporters of fluoridation are justified, whether this procedure is practical, and whether there are valid objections to the procedure are therefore highly relevant and demand our attention. Fluoridation of water supplies is put forward as being the cheapest and by far the most efficient means of ensuring that everyone receives

[7] Published in December, 1958.

[8] *Lancet*, 1960, 1: 1409 (June 25).

the fluoride which most of us lack. Alternative ways of providing fluoride have been considered and widely discussed. The taking of fluoride tablets, fluoridated toothpaste, fluoridized salt and the use of fluoride mouth-washes have all been suggested, and have their place in certain circumstances. Some doctors in Australia give their antenatal patients fluoride tablets,[9] and we understand that this is the practice of Professor Gordon King in the Department of Obstetrics of the University of Western Australia. This at least gets the new arrival off to a good start, but it is only a start. A little consideration will make it clear that most of these alternatives would make little impact on the problem as a whole, whatever they may do to the individual, and none can be considered an adequate alternative to fluoridation of the public water supply.

After perusal of all the evidence, a visitor from outer space might well be excused for asking what all the fuss is about. However, the fact remains that in the minds of some people fluoridation has become emotionally charged in such a way that objective judgement is difficult. For this reason the medical profession, which has a public duty to give objective advice in matters of this sort, has an obligation to keep itself adequately informed of the facts.

Comments and Abstracts.

MIGRATING BIRDS AND THE SPREAD OF DISEASE.

THE rôle of birds in the spread of disease is already familiar to medical scientists working in Australia. The probability that migrating birds are responsible for the periodic introduction of Murray Valley encephalitis into South Australia is now generally accepted. The vector responsible for the transfer of this disease from birds to man and to his animals is in this case believed to be a mosquito. However, birds have been implicated in a rather different rôle as possible agents in the spread of disease by work recently done in Egypt, where H. Hoogstrall and his colleagues[1] have been studying the ticks found on migrating birds. For the benefit of Australian readers it should be mentioned that the Nile Valley is one of the great "flyways", through which passes a substantial proportion of the vast numbers of migrating birds which every spring and autumn move between their breeding grounds in Europe and Western Asia, and their winter quarters in Africa south of the Sahara. The rôle of ticks as vectors of disease is of course well known; diseases in the transmission of which they have been implicated include tick typhus, "Q" fever, and a variety of other conditions of medical or veterinary importance. An important feature of many tick-borne diseases is that the pathogen may be transmitted through the egg from one generation to the next, so that the larvæ from the eggs of an infected tick may also be infected, without having come into contact with an infected vertebrate host. In tick-borne diseases birds may therefore be involved as the passive carriers of infected larval ticks, without being directly implicated in the propagation of the pathogen. In contrast to their rôle in the spread of mosquito-borne viruses, in which case birds carry the virus in their blood from the mosquitoes in one area to those in another, in the case of tick-borne infections birds may carry the infected tick from one region to another.

The tick species with which Hoogstrall has been mainly concerned is *Hyalomma marginatum*. This has two important sub-species, one European and one African, both known as reservoirs and vectors of organisms pathogenic to man and animals. It is also particularly well adjusted to make use of avian transport facilities, as it often behaves as a two-host tick, the larval stages feeding on birds, while the adults are usually found on the larger domestic and other mammals. Larval ticks remain on their avian hosts for at least two weeks, and may stay for six weeks or more, so when one attaches itself to a bird at the beginning of its migration, it may be carried for literally thousands of miles. There is corroborative evidence that this actually happens both in the recovery of ticks from migrating birds, and in the finding of occasional specimens, or even established populations of ticks, at places far outside their normal range. In his latest paper Hoogstrall reports having obtained 1025 immature ticks from 340 migratory birds. Twenty-two different species or subspecies of birds were involved, and in some species of which considerable numbers were examined, 15% to 20% of all birds examined carried ticks. There can therefore be no doubt that quite large numbers of potentially infected African ticks are distributed every spring by this means over a wide area in Europe and Asia.

It is true that bird movements may be responsible for the periodic appearance of a disease in an area where it cannot maintain itself permanently, as in the case of Murray Valley encephalitis, and it is possible that they may on rare occasions be responsible for the introduction of a disease into a new area. (It has been suggested that Kyasanur Forest disease, a tick-borne virus infection which made a sudden appearance as a new disease in the Mysore province of India a few years ago, could be a case in point.) However, it should be remembered that this is a process which has been going on from time immemorial, that the limits of distribution which any tick species could attain by such means have long ago been reached, and that the most this process can achieve is to reinforce existing populations or to deposit the ticks in areas where they cannot permanently survive. If a tick-borne disease succeeds in establishing itself in a new area, it is because conditions in that area have been changed; infected ticks will have been brought to that area many times before. Nevertheless, work of the kind reported by Hoogstrall, in addition to its intrinsic interest to scientists in a variety of disciplines, is a valuable contribution to a proper understanding of the epidemiology and distribution of tick-borne diseases.

TUTORING THE BRAIN-INJURED CHILD.

THE problems associated with the education of the brain-injured mentally retarded child have only recently begun to receive the attention which is their due. We therefore welcome a useful addition to the literature on this subject by Professor J. J. Gallagher,[1] in a book which describes, in very readable terms, an experiment conducted in the Dixon State School, Dixon, Illinois, in which the results of individual tutoring of certain brain-injured mentally retarded children were evaluated by a skilled team. Professor Gallagher was interested to find out whether one hour per day of such intensive tutoring for a period of 21 months could produce results not obtainable through group instruction. The observation was then continued for another year, after the intensive tutoring had been stopped for the first group, but made available to a second group. It should be noted that all the children in this experiment had suffered their injury before the age of three years, and so had had little opportunity for normal intellectual growth.

Important features of the experiment have been to test the theories that intellect develops through experiences,

[9] MED. J. AUST., 1960, 2: 956 (December 10).
[1] *Bull. Wld Hlth Org.*, 1961, 24: 197 (No. 2).

[1] "The Tutoring of Brain-Injured Mentally Retarded Children", by J. J. Gallagher, Ph.D., and with a foreword by S. A. Kirk, Ph.D.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications Ltd. 9" × 6", pp. 210. Price: 56s. (English).

in addition to maturation, and that changes affecting the reticular brain-stem can cause imbalance in the power of attention and concentration and so drastically reduce the process of learning.

Briefly, it can be stated that the study has demonstrated that improvement in the intellectual development of some brain-injured mentally retarded children can be obtained by such intensive tutoring; that the response was greater in achieving verbal than non-verbal skills; that the younger children (8 to 10 years) showed significant improvement over the older children (10 to 12 years); and that increased power of attention was noteworthy. However, it was observed that on the cessation of tutoring there was a tendency for the child's development to regress to lower levels or become arrested, and also that the individual variation was impressive.

Professor Gallagher's detailed description of tutoring techniques and of evaluation is of considerable practical interest. Perhaps the most important conclusion from this book is that we may have under-estimated the capacity for intellectual development of these children, and that the intensive methods described may give new hope to parents as well as to physicians and educationists. Further work along these lines and on a greater scale is indicated.

SHORTER ABSTRACTS.

SURGERY.

EARLY POST-OPERATIVE BATHING. C. J. Heifetz, *Arch. Surg.*, December, 1960.

THE author states that the simplification of post-operative care continues to be a highly desirable goal for surgeons. He describes a selected group of 100 patients with 107 clean, well-coaptated surgical wounds, whose dressings were left off altogether, or whose dressings were removed on the first or second post-operative day, and who were allowed to take a full shower or tub bath, daily, starting on the second or third post-operative day. Exposure of these wounds to routine bathing and drying seemed to have no adverse effect on healing. The author considers that early post-operative bathing simplifies post-operative care, reduces the work load of the hospital personnel, and cleanses the skin better than the routine bed bath.

HEALING COMPLICATIONS WITH PLASTIC ARTERIAL IMPLANTS. R. F. Smith and D. E. Szilagyi, *Arch. Surg.*, 1961, 82: 14-23 (January).

THE authors point out that defective healing of wounds in arterial surgery has always been attended by very serious consequences. They reviewed 343 vascular operations with plastic prostheses, and found 16 healing complications in 835 wounds and 39 healing complications in 852 anastomoses. The superficial wound infections, of which there were three instances, responded well to routine measures of antibiotic therapy and wound care. The results of the 11 deep wound infections were much less favourable. In about half the cases, serious hæmorrhage occurred and the mortality rate from complicating septicæmia for this group was 37·5%. The authors state that, although when the suture line is not involved in the infective process occasionally antibiotic therapy or drainage, or a combination of both, may bring about healing, in most cases of deep wound infection the only correct treatment is the removal of the prosthesis. They found that a post-operative false aneurysm was usually recognized clinically as a pulsatile swelling at the anastomotic line; at times it was observed only in the post-operative angiogram. Among the 32 false aneurysms encountered, rupture was a complicating feature of seven. The most common site for this lesion was the common femoral artery. Structural disease of the arterial wall at the site of anastomosis, defective suturing, faulty prosthesis and deep wound infection were the ætiological factors encountered, in that order of frequency. The most successful method of treatment of anastomotic false aneurysms was excision of the segment of the prosthesis bearing the lesion, with replacement by a new segment of plastic implant. The authors state that with this type of repair the patency of the implants could be preserved in over half of the cases. When serious hæmorrhage occurs, either from a false aneurysm or from a defective line of suture, the first consideration is to save the patient's life by stopping the hæmorrhage. The authors state that, although reconstructive repair is at times possible, the ligation of the prosthesis is usually mandatory.

SCHÖNLEIN-HENOCH SYNDROME. J. T. Phelan, *Surgery*, 1961, 49: 317-321 (March).

THE author reports five cases of Schönlein-Henoch syndrome in children. He points out that the surgical features of this disease are concerned with the gastro-intestinal tract, in that a surgical emergency may be simulated or may even actually occur, as the disease of the bowel may cause small-bowel intussusception. He points out that the cause of this condition is perivasculitis with its associated cellular extravasation, though the exact cause is unknown.

MAMMARY INFARCTS ASSOCIATED WITH PREGNANCY PRESENTING AS BREAST TUMOURS. J. Hasson and C. Pope, *Surgery*, 1961, 49: 313-316 (March).

THE authors report three cases of infarcts of physiologically hyperplastic mammary tissue appearing in association with pregnancy. In two cases the lesions appeared in the last month of pregnancy, and in one case during the first week of the puerperium. The lesions presented as discrete breast tumours which were excised for diagnosis. The authors point out how such conditions can simulate carcinoma of the breast, and how important it is to differentiate these lesions in order to avoid unnecessary radical operations.

EVENTRATION OF THE DIAPHRAGM. E. Michelson, *Surgery*, 1961, 49: 410-420 (March).

THE author discusses eventration of the diaphragm, illustrating his discussion with four representative cases of infantile and adult types of eventration. He states that eventration of the diaphragm is best classified clinically as infantile or adult in type. Infantile eventration may be congenital or acquired, is usually accompanied by serious respiratory distress, and should be treated surgically. He points out that operation is curative and the risk is minimal. The adult type of eventration is usually an acquired disease secondary to pneumonia, pulmonary infarcts, thoracic and abdominal operations and inflammation of the gall-bladder. He states that the diaphragm may remain temporarily or permanently paralysed, or may incompletely recover with partial paralysis. Symptoms may be either respiratory or digestive, and when symptoms persist and are well defined, surgical correction is indicated. High elevation of the diaphragm greatly diminishes the ventilation and oxygen uptake of the lung on that side, and mediastinal shift impairs the function of the contralateral lung. Surgical restoration of the paralysed diaphragm to its normal position will prevent mediastinal shift and produces almost normal ventilation and oxygen uptake. The author points out that repair of eventration of the diaphragm consists of excising or shortening the area of weakness, and thereby restoring it to the position of mid-respiration. The route used may be either transthoracic or transabdominal. The inelastic or redundant tissue may be retracted with forceps, overlapped, plicated or inverted with a series of purse-string sutures. Some surgeons resect the weakened areas, but branches of the phrenic nerve may be damaged. Partial eventration of the diaphragm may be congenital and associated with extralobar sequestration and/or perforating systemic vessels. Both congenital and acquired partial eventrations, like the small hernial sac, may incarcerate the bowel or liver and should be repaired. The author finally points out that eventration of the diaphragm is neither rare nor asymptomatic, and treatment is indicated in specific asymptomatic as well as symptomatic patients.

ONE OR TWO STAGE CERVICAL ESOPHAGOCOLOSTOMY OR ILEOSTOMY FOR REPLACEMENT OF THE ESOPHAGUS. P. Chrysospathis *et alii*, *Surgery*, 1961, 49: 429-431 (April).

THE authors report having operated on 21 patients in whom they used the colon to replace the œsophagus. In 10 patients the operation was performed for cicatricial damage and in 11 for cancer of the œsophagus. They performed an end-to-side anastomosis of the intestine with the cervical part of the œsophagus to the bowel, and the end of the colon or ileum was then implanted in the side of the neck to allow the introduction of a feeding catheter into the stomach or jejunum. They consider that this

method offers several advantages during the early post-operative period, and they think also that it simplifies the operative technique. They state that the immediate and late results of replacement of the œsophagus by this method were excellent.

THE PERPLEXING DUODENAL DIVERTICULUM. T. W. Jones and K. A. Merendino, *Surgery*, 1960, 48: 1068-1084 (December).

THE authors review the literature and their ten-year experience with the management of 49 patients with duodenal diverticula. They present a case of a symptomatic diverticulum producing common bile-duct compression and jaundice. They consider that the most common type of duodenal diverticulum is primary or acquired, occurring most commonly along the postero-medial aspect of the second part of the duodenum near the ampulla of Vater. They state that about 10% of these diverticula become symptomatic and can mimic any of the diseases of the abdomen. In a patient with symptoms and with a duodenal diverticulum, they consider that all other more common lesions must be ruled out as a source of the symptoms. If no other lesion can be found, and if the symptoms are unrelieved by medical measures, they consider surgical therapy is indicated. About 1% to 5% of these patients come to operation because of persistent intractable symptoms or, rarely, because of a serious complication secondary to pathological changes in the diverticula or to pressure from the diverticula. The authors consider that resection of the diverticulum is preferable, although sometimes inversion of the sac may be necessary. The mortality rate for resection varies between 5% and 10%. Death is generally due to injury of the ampulla of Vater or to a duodenal fistula.

TUMOR SIZE, DURATION OF SYMPTOMS, AND PROGNOSIS IN CARCINOMA OF THE BREAST. S. W. Gray *et alii*, *Surgery*, 1961, 49: 143-148 (February).

THE authors have considered the size of breast tumour and duration of symptoms among 289 patients, and have related this to age, survival and prognosis. They state that about 40% of the tumours, regardless of size, were discovered within one month prior to operation. Fewer than 5% of those under 2 cm. in diameter had persisted for one year or more. They consider that older patients sought treatment more promptly after discovery of a tumour than did younger patients, so that their tumours tended to be smaller and their survival time longer. Patients who died with cancer of the breast within five years after operation had at operation a significantly larger percentage of tumours over 4 cm. in diameter than did patients who lived for more than five years. The authors state that no patient free from disease five years after operation had a tumour over 6 cm. in diameter. Among patients in their series known to have died of cancer, the survival time was from 18 to 24 months longer when the tumour was less than 4 cm. in diameter at operation than when it was larger. Five-year survival rates of patients with the smaller tumours was 25% and with larger ones 5·9%. The authors consider that the size of the tumour at operation appears to be of much greater prognostic value than the duration of the tumour prior to operation.

SURGICAL ASPECTS OF INFRAPAPILLARY DUODENAL TUMORS. D. C. Higgins *et alii*, *Surgery*, 1961, 49: 149-160 (February).

THE authors point out that primary duodenal tumours, apart from those arising in the region of the duodenal papilla, are extremely uncommon. This report concerns a study made at the Mayo Clinic of 30 cases in which tumours of the infrapapillary portion of the duodenum were encountered surgically. Twenty-four of these tumours were malignant and six were benign. Four of the benign neoplasms were found incidentally, whereas bleeding was the cardinal symptom of the other two. All were removed readily with satisfactory results. Of the patients with malignant lesions, 21% were aged under 50 years. The average duration of symptoms was 14 months. In 59% of these cases the chief symptom was that of obstruction, and only 36% of the patients in this group presented resectable lesions. Bleeding was the prime symptom in 33% of the 24 patients with malignant lesions, yet three-quarters of these tumours were still resectable. In only 8% of the patients was pain the chief symptom. Pallor, or a palpable mass, or both, made up the only significant physical findings in the group with the malignant tumours. In 20% of the patients, the results of physical examination were normal. No patient was jaundiced at any time. X-ray studies were helpful in the diagnosis of malignant neoplasms, and a lesion in the infrapapillary part of the duodenum was reported in 91% of the patients. Only half of the malignant tumours were resectable. Segmental resection was performed in 10 cases and radical pancreato-duodenectomy in two. Eight of the specimens showed no involvement of the lymph nodes. Malignant invasion of the pancreas was proved in only one of the specimens from the patients on whom pancreato-duodenectomy was performed. One-third of the patients who had resection were alive and well five to 19 years after operation for the malignant tumours, and all of these had undergone segmental resection only. Twelve, or 50%, of the malignant lesions were beyond surgical resection. In 10 of the cases, palliative by-passing procedures were performed to relieve obstruction. One of the patients died in the immediate post-operative period, and 10 others were dead within two years.

BLEEDING ŒSOPHAGEAL VARICES IN CHILDREN. F. A. Arcari and H. B. Lynn, *Surg. Gynec. Obstet.*, 1961, 112: 101-105 (January).

THE authors present the information gained from the study of 75 cases of bleeding œsophageal varices. Fifteen of these were available for study in their own hospital and 60 were found in the literature. In the majority of instances it is difficult to establish the cause of the portal hypertension with bleeding varices in children. However, the site of the obstructive process responsible for the development of portal hypertension and its sequelæ was predominantly extrahepatic and in the portal venous system itself. The first bleeding episode occurred before seven years of age in more than 70% of the children in this series; this is a factor of considerable importance in the surgical management of the disease when it is realized that spleno-renal shunt is rarely successful in children under 60 or 70 pounds in weight (about 10 years of age), because of the small size of the shunt and therefore the high incidence of thrombosis. No patient died during the first bleeding episode. Of 42 patients followed up to a second bleeding episode without surgery, only one died of the second hæmorrhage and that six years after the first hæmorrhage. The low mortality during the first and second bleeding episodes makes it possible to delay operation, at least until after the second episode. Despite the low initial mortality, there was a 21% mortality among 28 patients followed up for three years without surgery. Operative treatment appears to be an essential part of the successful management of portal hypertension with recurrent bleeding from œsophageal varices. Emergency operations appear to be unnecessary and unwise in this condition. Splenectomy is not an effective method of handling bleeding œsophageal varices with portal hypertension. The most satisfactory method of achieving portal systemic decompression is spleno-renal shunt. A porta-caval shunt is rarely possible because the site of the obstruction is frequently at the portal vein. Probably the two procedures of value are ligation of the œsophageal varices or œsophago-gastrectomy with colon interposition. The authors consider that œsophago-gastrectomy with interposition of the colon may prove to be a satisfactory and definitive method of handling those children too small for a successful spleno-renal shunt or those children whose prior operation makes spleno-renal shunt impossible.

FAMILIAL ADENOMATOSIS OR POLYPOSIS: REPORT OF A CASE. C. W. Mayo, *Proc. Mayo Clin.*, 1960, 35: 409-413 (July 6).

The author reports a case of polyposis of the colon which he believes to be the first planned effort to preserve the rectum and sphincter muscles in a patient with multiple adenomatosis. It had been agreed that if a patient would undertake to have reexaminations of the remaining portion of the colon and rectum at six-month intervals to permit fulguration of any polyps which might develop, such a conservative policy would be justified. The patient was first seen in 1935. A subtotal colectomy was performed in stages, and thereafter the patient was seen about twice a year, and any polyps which were found were fulgurated. The patient is alive and well at the age of 64 years. The author concludes that end-to-end anastomosis between the ileum and the upper portion of the rectum or lower portion of the sigmoid colon, within reach of the sigmoidoscope for inspection of the anastomosis, is preferable to any other type of anastomosis, with a view to future care. Details of the procedures adopted are discussed.

Brush Up Your Medicine.

HAZARDS OF ANTICONVULSANTS.

THE following article has been prepared by the Special Therapeutics Committee appointed by the Council of the New South Wales Branch of the British Medical Association.

Phenobarbital and phemitone ("Prominal") produce drowsiness in overdoses. In a few patients, depression or irritability occurs, and occasionally marked excitement and over-activity, particularly with phenobarbital. Headache is occasional, and a widespread maculo-erythematous rash is an uncommon sensitivity reaction. Megaloblastic anæmia rarely occurs.

"Dilantin" (phenytoin sodium) in overdosage causes ataxia and drowsiness. Prolonged use in quite a lot of patients causes hypertrophy of the gums, sometimes sufficient to necessitate withdrawal of the drug. Gastric irritation and skin rashes occasionally occur.

"Mysoline" (primidone) in overdosage causes drowsiness and ataxia. It is common for these symptoms to be present in the first few days and then to disappear, and so gradual introduction of the dose is usually wise. Tolerance varies greatly, and some patients are so affected by small doses that the drug cannot be used, while others tolerate very big doses with no drowsiness or ataxia at all.

"Tridione" (troxidone), "Paradione" (paramethadione) and "Malidone" (aloxidone) occasionally cause drowsiness, irritability, photophobia or "glare phenomenon", bone-marrow depression, nephrosis and skin rashes. The "glare phenomenon", in which objects appear to glisten, is nothing but a nuisance, and is probably more common with "Tridione". Bone-marrow depression is rare, but serious, and can be fatal. Granulocytopenia or pancytopenia can occur. Patients must be warned to report fever, unusual pallor or a purpuric rash at once. Many people recommend that a leucocyte count should be done monthly in the first six months of treatment, and then less often for the next six months. If the neutrophil count falls below 1600 per cubic millimetre, weekly counts should be done. If it falls below 1000 or if the platelets as well as the neutrophils are reduced in numbers, the drug must be suspended. Nephrosis can be serious, but tends to disappear when the drug is withdrawn. Skin rashes vary, but occasionally serious exfoliative dermatitis has developed. Any marked skin rash calls for a change of drug, and very often one of the other drugs of this group is tolerated without the occurrence of a rash.

These drugs are used for the *petit mal* group of seizures. If one of them produces a serious toxic effect (marked bone-marrow depression, nephrosis or exfoliative dermatitis), it is wise to see whether an unrelated drug like "Milontin" will control the patient's seizures. If, on the other hand, the toxic effect has been mild or not potentially dangerous, another drug of this group can be tried and may be well tolerated.

"Milontin" (phensuximide), also used for *petit mal*, occasionally causes hæmaturia, either macroscopic or microscopic. This clears when the drug is suspended.

RELAXANTS.

THE following article has been prepared by the Special Therapeutics Committee appointed by the Council of the New South Wales Branch of the British Medical Association.

The relaxants in use today offer many advantages to patients, surgeons and anæsthetists in providing excellent operating conditions without the considerable general metabolic disturbances associated with the traditional inhalation anæsthetic agents. However, their use is not without danger, unless the anæsthetist properly appreciates their pharmacological properties and the possible complications that may ensue during or after their administration.

Although they are convenient to administer, their safe use requires experience with the careful and thorough application of basic anæsthetic principles. They are not drugs to be used by the tiro or occasional anæsthetist.

Division of relaxants according to mode of action into depolarizing and non-depolarizing groups has practical significance. Non-depolarizers, like tubocurarine, on repeated administration continue to have the same mode of action which is reversed by neostigmine. Depolarizers, like succinylcholine, have no satisfactory antidotes; on repeated administration they may exhibit tachyphylaxis and later begin to act like non-depolarizers—a dual or mixed block. The availability of an antidote and reliability of action are definite advantages of the non-depolarizers.

As the side effects of relaxants are infrequent, the other main consideration in choosing one or the other is the duration of action required. General points considered in choosing between the four most popular relaxants are set out in Table I. The paramount danger associated with their use is indicated at the bottom of this table.

TABLE I.

	Non-Depolarizing Relaxants.		Depolarizing Relaxants.	
	Tubocurarine.	Gallamine.	Decamethonium.	Succinylcholine.
Antidote	Neostigmine.	Neostigmine.	—	—
Mixed block	No.	No.	Yes.	Yes.
Duration	30 min.	20 min.	15 min.	5 min.
Side effects	Hypotension, bronchospasm.	Tachycardia.	Muscle pains (rarely).	Muscle pains, hypertension.
Danger	Asphyxia.	Asphyxia.	Asphyxia.	Asphyxia.

Altered Sensitivity to Relaxants.

There may be an increased or altered sensitivity to relaxants in certain circumstances. These circumstances may be regarded as relative contraindications to their use: (*a*) in states of oligæmia, dehydration, electrolyte imbalance and emaciation; (*b*) in cases of respiratory obstruction and insufficiency; (*c*) during the inhalation of potent anæsthetics such as ether and halothane; (*d*) in severe hepatic and renal disease; (*e*) in neonatal anæsthesia; (*f*) after "Pitocin" infusions in obstetrics; (*g*) in myasthenia gravis or carcinomatous neuropathy.

Mixing Relaxants.

As a rule it is unwise to combine depolarizing and non-depolarizing agents, because abnormal responses may result. The only exception to this rule is the use of single doses of succinylcholine for intubation, which may be followed, after the patient has commenced to breathe again, by a non-depolarizing agent in divided doses for the remainder of the operation.

Depolarizing drugs should not be used for peritoneal closure after previous doses of non-depolarizing agents. This will avoid the possibility of some abnormal response causing prolonged paralysis and apnœa.

Antidotes to Relaxants.

The first treatment in persistent paralysis is efficient artificial ventilation, and this is best performed with an endotracheal tube in place. A much better response will be obtained if the antagonist is administered when some recovery from the relaxant is apparent, and, further, excessive amounts of the antagonist will be avoided.

The paralysis due to a non-depolarizing agent is reversed by the anticholinesterase neostigmine. The large doses of neostigmine required for this may produce dangerous muscarinic side effects such as cardiac asystole and bronchorrhœa unless the patient is given atropine beforehand. Atropine, 1 mg., is injected intravenously. After at least three minutes, neostigmine is injected intra-

venously at the rate of 0·5 mg. per minute until muscle power returns. It should not be necessary to exceed 2·5 mg. of neostigmine.

Satisfactory antidotes to depolarizing agents are not available as yet.

Hazards of Relaxants.

Asphyxia.

The most frequent and dangerous hazard with relaxants is asphyxia due to inadequate pulmonary ventilation. Deaths attributed to relaxants are due directly to the deleterious effects of hypoxia on the heart and brain. Doses sufficient to paralyse the abdominal muscles interfere inevitably with tidal exchange.

A relaxant should never be given without full facilities for endotracheal intubation and intermittent positive pressure ventilation. After operation it is essential to ensure adequacy of tidal volume before allowing the patient to leave the operating theatre. The following three criteria are important for gauging the adequacy of tidal exchange: (i) expansion of the whole thoracic cage on inspiration; (ii) ability to raise the head and protrude the tongue; (iii) maintenance of a pink colour after breathing air for 10 minutes.

If there is any doubt, the patient should remain in the theatre block until muscle power returns, either spontaneously or after the injection of atropine and "Prostigmin".

The Facilitation Syndrome.

With the onset of muscle paralysis, the respiratory signs cease to be of value in assessing depth of anæsthesia. If artificial respiration is maintained with a potent inhalation anæsthetic, over-concentration will lead rapidly to depression of the circulation and death. The combination of a potent anæsthetic and a relaxant is not necessary, and should be avoided.

Prolonged Hypopnœa and Apnœa.

This is a problem with the use of relaxants, but life is not threatened if artificial respiration is maintained. The four main causes of prolonged apnœa at the end of operation are discussed briefly below.

Anæsthetic or Narcotic Depression.—This can occur only with the use of potent anæsthetics such as ether, cyclopropane and thiopentone, or of narcotics such as pethidine. It can be treated and/or excluded, either by hyperventilation to excrete gaseous anæsthetics, or by the injection of the antidotes to thiopentone and pethidine, "Bemegride" and allylnormorphine respectively.

Carbon Dioxide Narcosis.—Long-continued underventilation of the paralysed patient allows anæsthetic concentration of carbon dioxide to accumulate in the body. Inadequate absorption by soda lime in closed anæsthetic systems can accentuate this accumulation. It can be treated and/or excluded by a period of ventilation with fresh soda lime.

Respiratory Alkalosis or Habit Apnœa.—This is frequent if controlled hyperventilation is employed during the anæsthetic. Characteristically, there is no evidence of spontaneous respiration. The presence of "jaw tug" immediately suggests one of the other three causes. Habit apnœa ceases abruptly on brisk stimulation of the larynx with an airway, or after a brief period of underventilation.

Prolonged Neuro-Muscular Block.—If the other three causes of prolonged hypopnœa have been excluded, a persistence of neuromuscular block is likely, and may be due to one or more of the three following factors. (*a*) There may be continued action of non-depolarizing agents, such as curare; this is usually reversed by atropine and "Prostigmin", as was mentioned above. (*b*) There may be continued action of depolarizing agents, such as decamethonium; this paralysis is commonly short lived, and, as there is no antidote, artificial respiration must be continued till spontaneous recovery occurs. (*c*) There may be a dual response to depolarizing agents; this is likely after succinylcholine infusions, if repeated doses of succinylcholine are administered after non-depolarizing agents, and if more than 7·5 mg. of decamethonium are administered. A 10 mg. intravenous test dose of edrophonium rapidly but briefly reverses a dual block and intensifies a persisting depolarization block. In the former instance, atropine and "Prostigmin" are indicated, in the latter artificial respiration alone is required. The possibility of a dual response is considered reduced by confining the use of depolarizing drugs to short operations in which the initial dose only will be required, or for intubation prior to the use of non-depolarizing relaxants in longer operations.

Inhalation of Vomitus.

Regurgitation of gastric contents in unprepared patients (intestinal obstruction, obstetrics, trauma, etc.) may be facilitated by the sudden complete relaxation of the diaphragm following a dose of a relaxant. Accordingly, in these cases the relaxants are better avoided or used with extreme caution, and a cuffed endotracheal tube should always be passed.

Use of Relaxants for Cæsarean Section.

This is an extremely controversial subject. Some maintain that relaxants should not be used. It is impossible to reconcile experimental work with clinical practice. It would appear that in current practice succinylcholine and/or tubocurarine is used, the precautions detailed being observed above.

Out of the Past.

ROYAL NORTH SHORE HOSPITAL.[1]

[From the *Australasian Medical Gazette*, June 30, 1903.]

THE Royal North Shore Hospital of Sydney was officially opened on June 10th by Sir John See. The Premier was received by the president of the committee (Mr. J. Randal Carey) and shown over the buildings, which comprise an administrative block and one portion with isolated wards, kitchen and other very necessary adjuncts. Provision is made for the reception of about 50 patients, but a completion of the design accommodation will be found for upwards of 160 patients . . . Sir John See expressed the pleasure it gave him to declare the hospital open for the reception of patients. He paid a tribute to the hospital management, and congratulated the committee on the magnificent edifice that had crowned their efforts. He congratulated the medical men of the State on their ungrudging and uncomplaining services given for the benefit of suffering humanity, and he added that in this connection the nurses should not be forgotten, as in the successful management of any hospital it had been clearly shown that their services were as completely necessary as those of the medical profession. To give the best results it was imperative to provide buildings complete in detail with a due regard to sanitation, ventilation and light, so that the spread of disease could be successfully combated.

Medical Societies.

THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A MEETING of the Medical Sciences Club of South Australia was held on September 5, 1961, at the Tutorial Room, Anatomy Department, University of Adelaide.

Chromatographic Studies of the Circulating Thyroid Hormones.

DR. M. L. WELBY reported the results of studies of the circulating thyroid hormones. He said that paper chromatographic techniques for the study of the pattern of the

[1] From the original in the Mitchell Library, Sydney.

thyroid hormone in the blood had been developed and had confirmed the classical concept that thyroxine and small amounts of triiodothyronine were the only hormones circulating in normal subjects in the basal state. However, in addition he presented evidence indicating that in states of thyroid stimulation—for example, after the administration of thyrotropic hormone and also in hyperthyroidism—significant amounts of the iodotyrosines were released into the plasma, in addition to an increased amount of triiodothyronine. The significance of the findings was briefly discussed.

The Pattern of Erythrocyte Destruction in Hæmolytic Syndromes.

DR. H. LANDER reported a study of the site of destruction of red cells in 84 patients suffering from a variety of hæmolytic syndromes. Red cells from each person studied were labelled with radio-chromium by the method described by Mollison Veall in 1955 and reinjected into the patient. Subsequently, the chromium half-time was determined, and the site of sequestration of the red cells was found by external scintillation counting over a number of organs. In each case measurements were performed over the heart, liver, spleen, sacrum (marrow) and lungs. In a few instances, measurements were also performed over large tumour masses. Four major patterns of radio-chromium uptake with respect to those organs emerged. In Type I, no significant uptake occurred. There was a steady fall-off in activity in all organs counted. In Type II, uptake occurred only in the liver. In Type III, uptake occurred in both the liver and the spleen. (In such cases there might be either (*a*) hepatic or (*b*) splenic predominance.) In Type IV, uptake occurred only in the spleen. Sub-varieties of that pattern were described. Dr. Lander said that evidence had also been accumulated which suggested that under certain pathological conditions the bone marrow, and perhaps also the lungs, might become a major site of red-cell destruction in the body. The clinical implications of the studies, with particular respect to the operation of splenectomy, were discussed

British Medical Association.

VICTORIAN BRANCH.

The Sir Richard Stawell Oration.

THE 28th Sir Richard Stawell Oration will be delivered on Wednesday, November 1, 1961, by R. W. T. Cowan, M.A., B.Litt. (Oxon.), Warden of Trinity College, Melbourne. The title will be "Some Problems of our Expanding Universities".

Correspondence.

NOTES ON THE USE OF "CATOVIT" IN RELATION TO CHRONIC ALCOHOLISM.

SIR: During the past twelve months I have had occasion to use "Catovit" (C. H. Boehringer Sohn) fairly extensively in the chronic alcoholic.

There are certain definite recognizable phases which every chronic alcoholic passes through for a matter of three to five years following the cessation of his drinking. These phases occur in the early stages of this period frequently, and with varying degrees of intensity; both are related to the physical and mental states and occur invariably in the chronic alcoholic. On the physical side, ease and frequency of muscular fatigue may occur without warning, and may or may not be associated with muscular effort. The patient feels a complete physical let-down which is extremely real, and which on physical examination provides no signs of organic disturbance. It is generally a separate entity and occurs usually in association with the mental fatigue which is also a feature. When this state occurs, it is easy to see that in the chronic alcoholic he is most likely to return to alcohol, and it is for this reason that I prescribed "Catovit" because of the twofold effect of this product. Phenylpyrrolidino-pentane hydrochloride overcomes the apathy and mental fatigue, and the vitamin content of this product supplies a quick replacement of what may possibly be a sudden vitamin deprivation.

For the first three months after the cessation of alcohol, I prescribed "Catovit" daily at a dosage of three tablets per day. This I feel sure, forestalls the frequency and severity of these strange mental and physical let-downs of the post-alcoholic. After this period they are instructed to take "Catovit" when they are aware of this predescribed condition. I have no fear, and have not encountered any signs of addiction with this product in this type of patient. This is most rare, because of the inherent nervous disorder which has led them to become addicted to alcohol. It cannot be compared to the stimulation such an individual gets from, e.g., "Benzedrine" or alcohol.

I have found "Catovit" to be a useful adjunct in the treatment of chronic alcoholics.

Yours, etc.,

P. H. SPEIGHT.

The Langton Clinic,
Dowling Street,
Moore Park, N.S.W.
August 31, 1961.

RESPIRATOR UNIT, SYDNEY HOSPITAL.

SIR: Sydney Hospital has established recently a respirator unit for the intensive care of patients with respiratory paralysis. The unit is designed for the management of patients with weakened or paralysed breathing, no matter what the cause. Frequently this respiratory weakness and resultant pneumonia cause death in otherwise recoverable diseases. Cases already treated successfully have been poliomyelitis, acute ascending polyneuritis (ascending paralysis), barbiturate or other intoxication, tetanus involving the use of paralytic drugs, virus encephalitis and the crises of myasthenia gravis.

The respirator unit is served by a team of doctors from medical, surgical and anæsthetic services, and a 24 hours a day roster of both resident medical and nursing staff is arranged. The routine includes repeated chest, neurological and general examinations to assure tracheostomy and artificial respiratory aid as early as possible in the prevention of pneumonia and anoxia. A wide range of respirators is now available to provide for the requirements of different patients.

Medical practitioners having problems of this kind are invited to telephone the Medical Superintendent of Sydney Hospital, who will arrange for advice to be given regarding urgent treatment, management and admission.

Yours, etc.,

NORMAN ROSE,
Medical Superintendent.

Sydney Hospital,
Sydney.
September 4, 1961.

A UNIQUE USE FOR "TACE".

SIR: The sexual perversions in men (homosexuality, exhibitionism, fetishism, etc.) present a psychiatric and social problem of some magnitude, which is very difficult and often unrewarding to treat. These people can often be helped by the use of drugs which diminish their libido, the rationale of such treatment being that, if their sexual drive is diminished, then their socially-unacceptable behaviour will diminish and sometimes disappear.

The drug usually used is stilbœstrol (from 5 to 15 mg. per day). However, the dose of such an œstrogenic drug is so high that it causes many untoward and unpleasant side effects—e.g., nausea, but more importantly, enlargement and tenderness of the breasts. This often causes so much discomfort and embarrassment that these patients often refuse taking the prescribed medication.

In several such patients I have replaced the stilbœstrol by "Tace", which the manufacturers claim does not give rise to gynæcomastia, and have found that this claim is substantiated. Although I have used "Tace" in only three cases, it has had the same effect in all—namely, that the breast enlargement and, to a lesser extent, the tenderness has diminished with no resurgence of libido. In all cases the dose has been two capsules daily, but on theoretical grounds may be reduced still further later on, as it is said to form a depot in the body fat.

Yours, etc.,

BILL ROWE.

149 Macquarie Street,
Sydney.
September 1, 1961.

Royal Australasian College of Surgeons.

PRIMARY EXAMINATION FOR FELLOWSHIP.

A PRIMARY EXAMINATION in anatomy (including normal histology) and applied physiology and the principles of pathology, will be conducted in Melbourne in March, 1962, for the fellowship of the Royal Australasian College of Surgeons. The written papers will be held on Thursday and Friday, March 1 and 2, 1962. The viva-voce sections of the examination will commence on Monday, March 5, 1962. The examination is reciprocal with the primary examination for fellowship of the Royal College of Surgeons of England, the Royal College of Surgeons of Edinburgh and the Royal College of Surgeons in Ireland, or the primary examination in surgery of the Royal Faculty of Physicians and Surgeons of Glasgow and The College of Physicians, Surgeons and Gynæcologists of South Africa. Each examination is open to graduates of not less than one year's standing of a medical school approved by the Council of the College for the purpose.

Candidates must submit evidence of their qualifications and date of acquirement thereof. Forms of application for admission to the examination may be obtained from the Assistant Secretary, Royal Australasian College of Surgeons, Spring Street, Melbourne, C.1, Victoria. The fee for admission or readmission to the examination is £31 10s., plus exchange on cheques drawn on banks outside Melbourne. The fee must be forwarded with the form of application so as to reach the Assistant Secretary at his office in Melbourne not later than January 19, 1962. It is stressed that late entries cannot be accepted. Copies of the regulations governing examinations for fellowship are available on application.

FACULTY OF ANÆSTHETISTS.

Primary Examinations for Fellowship.

A PRIMARY EXAMINATION in anatomy, physiology, pharmacology and pathology will be conducted in Melbourne in March, 1962, for the fellowship of the Faculty of Anæsthetists of the Royal Australasian College of Surgeons. The written papers will be held on Thursday and Friday, March 1 and 2, 1962. The viva-voce sections of the examinations will commence on Monday, March 5, 1962. The examination is reciprocal with the primary examination for fellowship of the Faculty of Anæsthetists of the Royal College of Surgeons of England. Each examination is open to graduates of not less than one year's standing of a medical school approved by the Council of the College for the purpose. Candidates must submit evidence of their qualifications and date of acquirement thereof. Forms of application for admission to the examination may be obtained from the Assistant Secretary, Faculty of Anæsthetists, Royal Australasian College of Surgeons, Spring Street, Melbourne, C.1, Victoria. The fee for admission or readmission to the examination is £31 10s., plus exchange on cheques drawn on banks outside Melbourne. The fee must be forwarded with the form of application so as to reach the Assistant Secretary at his office in Melbourne not later than January 19, 1962. It is stressed that late entries cannot be accepted. Copies of the regulations governing examinations for Fellowship are available on application.

University Intelligence.

UNIVERSITY OF SYDNEY.

DR. D. C. MADDISON has been appointed Professor of Psychiatry at the University of Sydney.

UNIVERSITY OF NEW SOUTH WALES.

THE University of New South Wales announces the appointment of Mr. T. B. McMurray, M.B.E. (Military), to the position of Executive Officer for Post-Graduate and Extension Studies in Medicine. Mr. McMurray qualified in Liverpool in 1941. He joined the army early in 1942 and took part in the work of the Airborne Research Establishment at Sherborne. Later he commanded a parachute surgical team until he was wounded in action in 1945. On return to civil life he obtained the Fellowship of the Royal College of Surgeons of Edinburgh in 1946 and the degree of M.Ch.Orth. of Liverpool in 1947. In 1948 he joined the staff of the University of Capetown as Lecturer in Orthopædic Surgery. While in South Africa he was elected to the Branch Council of the South African Medical Association and one year later was elected to the Federal Council of the South African Medical Association on which he served until 1961. He was chairman of the Northern Areas Division of the S.A.M.A., secretary of the S.A.M.A. Committee on Medical Education, a member of the Workman's Compensation Committee, a member of the Central Committee on Contract Practice, and a member of the Military Appeals Tribunal for South Africa. In 1959, he represented South Africa at the World Congress on Medical Education in Chicago and at the World Medical Association and World Health Organization Conferences. He was secretary of the steering committee to establish the South African College of Physicians, Surgeons and Gynæcologists, and was subsequently appointed Honorary Registrar of the College, a post he held until he left for Australia. He served as examiner for the final fellowship examination in surgery of the South African College.

Notes and News.

Endorsement of B.S. 3263 Proposed.

The Standards Association of Australia announces a proposal to endorse B.S. 3263: 1960, Rubber Closures for Injectable Products, as an Australian standard, subject to amendments to suit Australian conditions. This standard lays down tests and requirements which ensure that the closures, with their appropriate seals, form an effective barrier against microorganisms after sterilization. The closures referred to are wads (flat rubber disks), plugs (with or without skirt or flange) and caps (rubber covers held in position on the outside containers by the tension of the rubber). They may be made from either natural or synthetic rubber and in a variety of formulations.

To produce suitable closures, various fillers, accelerators and antioxidants are mixed with the rubber before vulcanization. As a result, the miscellaneous closures will possess different properties, and this standard provides methods and limits with which closures intended for use with injectable products must comply. It has been found impracticable to prepare a standard to ensure compatibility of the rubber closures with the pharmaceutical products with which they are used. Instead, a test for compatibility should be carried out before a rubber mix is approved, and an appendix is included to provide a suggested standardized procedure for such a test.

The proposal to endorse B.S. 3263 is set out as Document 607. Copies of B.S. 3263 may be examined or purchased at the headquarters of the Standards Association of Australia, 157 Gloucester Street, Sydney, or at branch offices in the capital cities of all States and at Newcastle. Comment on Document 607 is invited from persons or organizations with experience in the manufacture or use of rubber closures. Such comment should reach the Association before November 30, 1961.

Services Canteens Trust Fund.

Higher Training Education Awards.

The trustees of the Services Canteens Trust Fund are inviting applications for education awards for post-graduate studies in auxiliary services to medicine, welfare and science, such as nursing (male and female), physiotherapy, speech therapy, occupational therapy, orthoptic therapy, laboratory technician. The awards will be granted for any full-time post-graduate course at the college or training centre selected, and will be tenable for the period prescribed for the course. Post-graduate nursing courses for which awards may be granted will be any approved course at the College of Nursing, Australia, or the New South Wales College of Nursing. Higher training education awards for physiotherapy, speech therapy, occupational therapy and orthoptic therapy, laboratory technician or other courses will be available for approved courses at training institutions in Australia accepted by the trustees for the purposes of

higher training education awards. The trustees will also consider applications for higher training education awards in the fields specified above at training centres overseas, provided such courses or equivalent training is not obtainable in Australia.

The value of higher training education awards will be determined by the trustees in each case, and will be designed to cover the costs involved in the course, such as fees, books and stationery required for the course, fares as necessary and a reasonable maintenance allowance.

Any person whose mother or father served in the Australian Armed Forces between September 3, 1939, and June 30, 1947, is eligible to apply for an award. Persons who themselves served in the Forces during the 1939-1945 war, but neither of whose parents served during the War, are not eligible.

The applicant must possess the qualifications prescribed by the college or training centre concerned to enter upon the course proposed. A formal academic qualification, such as leaving or matriculation certificate, is not essential, provided the applicant is in every way suitable and qualified to undertake the course proposed.

Applications must be made on the prescribed form, which can be obtained from the General Secretary or a Regional Secretary of the Services Canteens Trust Fund. Applications must be lodged with the General Secretary of the Services Canteens Trust Fund, Victoria Barracks, St. Kilda Road, Melbourne, not later than December 1, 1961, irrespective of the date the course proposed commences next year. The addresses of Regional Secretaries are as follows: Queensland, Victoria Barracks, Brisbane; New South Wales, 84 Pitt Street, Sydney; Victoria, Victoria Barracks, Melbourne; South Australia, 22 Grenfell Street, Adelaide; Western Australia, Swan Barracks, Perth; Tasmania, Anglesea Barracks, Hobart.

Trachoma.

The following statement has been issued by the Expert Committee on Trachoma of the World Health Organization.

Trachoma, and its associated eye diseases, is believed to affect more than 400,000,000 people on all continents. The World Health Organization's third Expert Committee on Trachoma was opened on August 29, 1961, by Dr. Pierre Dorolle, Deputy Director-General of WHO, in the Palais des Nations. Dr. John C. Snyder, Dean of the Harvard School of Public Health, was unanimously elected chairman of the meeting, Professor Ida Mann, of the Ophthalmic Research Institute of Australia, vice-chairman, Dr. J. Graham Scott, Johannesburg, South Africa, *rapporteur* (English), and Professor A.-M. Larmande, Director of the Institut de Trachomatologie, Algiers, *rapporteur* (French).

This third meeting of the Expert Committee on Trachoma was called at an important time in the history of the disease. Since the second, which was held in 1955, the causal agent of trachoma has been cultivated in the yolk sac of the chick embryo, and intensive laboratory research is now being carried out by groups of scientific workers in some 30 institutions throughout the world. This Committee considered the practical application of new advances in research to the problem of trachoma control. Other items on the agenda were recent advances in treatment suitable for mass application and the present status of immunology. The Committee also reviewed ways and means of extending pilot projects in trachoma control to wider population groups, and of integrating such measures into the general public-health services and community development programmes.

An Overseas Drug Company in Australia.

Farbenfabriken Bayer A. G., Leverkusen, West Germany, is to form an Australian subsidiary, FBA Pharmaceuticals (Aust.) Pty. Ltd., with headquarters in Sydney. The Managing Director is to be Mr. E. J. Willis, Federal President of the Australian Association of Ethical Pharmaceutical Industry.

International Congress for Hygiene and Preventive Medicine.

The third International Congress for Hygiene and Preventive Medicine will be held on May 26 to 30, 1962, at Vienna. The congress is being arranged by the International Federation for Hygiene and Preventive Medicine, with the collaboration of the International Atomic Energy Agency. The subject will be "Public Health and Protection against Radiation". There will also be a round-table conference on genetics, embryopathy and prenatal diseases. Further information may be obtained from the Secretary-General, Med.-Rat. Dr. Ernst Musil, Wien XV, Mariahilfer Strasse 177, Austria.

Naval, Military and Air Force.

APPOINTMENTS.

THE following appointments, changes, etc., are published in the *Commonwealth of Australia Gazette*, No. 66, of August 17, 1961.

AUSTRALIAN MILITARY FORCES.

Citizen Military Forces.

Northern Command.

Royal Australian Army Medical Corps (Medical).—The provisional appointment of 2144660 Captain R. G. R. Sim is terminated, 31st May, 1961.

Southern Command.

Royal Australian Army Medical Corps (Medical).—3157152 Lieutenant-Colonel J. E. Clarke is appointed from the Reserve of Officers and is appointed Consultant Physician, Army Headquarters, and to be Temporary Colonel, 29th June, 1961.

Reserve Citizen Military Forces.

Northern Command.

Royal Australian Army Medical Corps (Medical).—To be Honorary Captains—Robert George Robertson Sim, 1st June, 1961, and David Kenneth Barron Fraser, 17th July, 1961.

Citizen Military Forces.

Eastern Command.

Royal Australian Army Medical Corps (Medical).—526429 Lieutenant-Colonel K. W. H. Harris relinquishes command, 1st Field Ambulance, 20th May, 1961. The provisional appointment of 2130132 Captain R. F. Thew is terminated, 31st January, 1961.

Western Command.

Royal Australian Army Medical Corps (Medical).—The provisional appointment of 526689 J. T. Carroll is terminated, 20th May, 1961.

Reserve Citizen Military Forces.

Eastern Command.

Royal Australian Army Medical Corps (Medical).—To be Honorary Captain, 1st February, 1961—Roy Farley Thew.

Citizen Military Forces.

Eastern Command.

Royal Australian Army Medical Corps (Medical).—The provisional appointment of 262453 Captain K. D. Coulthurst is terminated, 27th February, 1961. *To be Captain (provisionally), 28th February, 1961*—262453 Keith Dudley Coulthurst.

Southern Command.

Royal Australian Army Medical Corps (Medical).—The provisional appointments of the following officers are terminated:—Captains 3111532 H. A. Marks, 3rd February, 1961, and 3101951 P. M. Birrell, 23rd February, 1961. *To be Captains (provisionally)*—3111532 Howard Alfred Marks, 4th February, 1961, and 3101951 Peter Matheson Birrell, 24th February, 1961.

The Royal Tasmania Regiment.—Royal Australian Army Medical Corps (Medical).—The provisional appointment of 615430 Captain J. D. Brennan is terminated, 25th November, 1960. *To be Captain (provsionally), 26th November, 1960*—615430 John Dermod Brennan.

Central Command.

Royal Australian Army Medical Corps (Medical).—To be Lieutenant-Colonel, 1st July, 1961—432070 Major (Temporary Lieutenant-Colonel) A. K. Grant.

Retired List.

Western Command.

The following officers are retired, 6th July, 1961:—Captains R. V. Pratt, M. A. Radcliffe-Taylor.

The following appointments, changes, etc., are published in the *Commonwealth of Australia Gazette*, No. 68, of August 24, 1961.

AUSTRALIAN MILITARY FORCES.

Citizen Military Forces.

Northern Command.

Royal Australian Army Medical Corps (Medical).—The provisional rank of 146882 Captain K. R. Townley is confirmed.

Eastern Command.

Royal Australian Army Medical Corps (Medical).—The provisional appointment of 2267200 Captain J. M. Purchas is terminated, 25th May, 1960. *To be Captain (provisionally), 26th May, 1960*—2267200 James Maurice Purchas.

Southern Command.

Royal Australian Army Medical Corps (Medical).—The provisional rank of 350275 Captain K. B. Layton is confirmed.

Central Command.

Royal Australian Army Medical Corps (Medical).—431935 Lieutenant-Colonel D. F. Hannon relinquishes command 3rd Field Ambulance, 30th September, 1961, and is seconded whilst in the United Kingdom, 1st October, 1961.

Western Command.

Royal Australian Army Medical Corps (Medical).—538113 Captain J. M. Hill and 526624 Captain (provisionally) G. N. Cumpston are seconded whilst in the United Kingdom, 31st July, 1961, and 1st August, 1961, respectively.

Reserve Citizen Military Forces.

Central Command.

Royal Australian Army Medical Corps (Medical).—Captain F. G. T. Turner is placed upon the Retired List (Central Command) and granted a military title equivalent to the substantive or honorary rank shown, with permission to wear the prescribed uniform, 31st August, 1961.

Australian Regular Army.

Royal Australian Army Medical Corps (Medical).—To be Colonel, 4th August, 1961—47545 Lieutenant-Colonel (Temporary Colonel) C. M. Gurner, E.D.—(Ex. Min. No. 73—Approved 17th August, 1961.)

The following appointments, changes, etc., are published in the *Commonwealth of Australia Gazette*, No. 69, of August 31, 1961.

AUSTRALIAN MILITARY FORCES.

Citizen Military Forces.

Northern Command.

Royal Australian Army Medical Corps (Medical).—The provisional rank of 139257 Captain R. L. G. Newcombe is confirmed.

Southern Command.

Royal Australian Army Medical Corps (Medical).—To be Captain (provisionally), 3rd August, 1961—355816 David Joseph Fitzgerald.

Reserve Citizen Military Forces.

Southern Command.

Royal Australian Army Medical Corps (Medical).—To be Honorary Captain, 4th August, 1961—Emanuel Wilder.

Post-Graduate Work.

THE MELBOURNE MEDICAL POST-GRADUATE COMMITTEE.

PROGRAMME FOR OCTOBER, 1961.

THE Melbourne Medical Post-Graduate Committee announces that the following courses will be conducted in October.

Overseas Visitors.

Mr. S. H. Wass, M.S., F.R.C.S., of London, will be guest surgeon to Prince Henry's Hospital from September 25 to October 20. A series of lectures and seminars have been arranged at the hospital, and details may be obtained from

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED AUGUST 19, 1961.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	2(1)	2(2)	2(1)	..	..	..	..	..	6
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	3	..	3
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	5(5)	1(1)	..	..	..	..	1	..	7
Diphtheria	..	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	4(1)	..	4(4)	1(1)	..	..	1	..	10
Encephalitis	1(1)	..	2(2)	..	..	..	..	..	3
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	120(54)	58(31)	9(1)	37(19)	9(4)	9	..	15	257
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	2	..	2
Leptospirosis	..	..	..	..	1	..	..	..	1
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	2(2)	..	..	..	..	..	..	..	2
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	1	..	2(1)	1(1)	..	..	1	..	5
Puerperal Fever	1	..	..	..	1(1)	..	..	..	2
Rubella	..	7(7)	..	1	1(1)	..	1	1	11
Salmonella Infection	..	..	..	..	1	..	..	..	1
Scarlet Fever	8(5)	11(8)	..	3(3)	..	2	..	..	24
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	10(9)	17(15)	3(1)	9(9)	6(3)	1	2	..	48
Typhoid Fever	..	1(1)	..	..	..	..	..	..	1
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

the Dean's Office, Prince Henry's Hospital, St. Kilda Road, Melbourne.

The Honourable Walter Symington Maclay, senior officer of the Psychiatric Board of Control, United Kingdom, will visit the Department of Mental Hygiene from October 16 to November 2, and will lecture on "Psychiatric Rehabilitation" for the Committee at 8.15 p.m. on Tuesday, October 24, in the Medical Society Hall.

Mr. Harold Dodd, F.R.C.S., of London, will make a brief visit to Melbourne at the end of October. He will lecture on "Venous Disorders of the Lower Limbs—A Unified Concept", at 8.15 p.m. on Monday, October 30, at the Medical Society Hall.

All members of the medical profession are invited to attend lectures by these visitors.

Symposium on Problems of Respiratory Failure and its Management.

Under the ægis of the University Department of Medicine, Royal Melbourne Hospital, a symposium on problems of respiratory failure and its management will be conducted on October 27 and 28, 1961. Full details were given in THE MEDICAL JOURNAL OF AUSTRALIA of August 26. No fee will be charged for attendance, but registration with the Committee is essential. Those wishing to attend should forward name and address, and indicate at which sessions they will be present and, in particular, whether dinner is required on the evening of Friday, October 27. Inquiries, other than those related to registration, may be directed to Dr. Bryan Gandevia, at the Royal Melbourne Hospital. Telephone: FJ 0266, Extension 461.

Country Courses.

Horsham.—On Saturday, October 7, in the Nurses' Lecture Room, Wimmera Base Hospital, Horsham, the following course will be given: 2.30 p.m., "The Surgery of Skin Cancer", Mr. J. T. Hueston; 4 p.m., "Recent Advances in Cardiology", Dr. H. B. Kay; 5.15 p.m., "Habitual Abortion", Mr. W. J. Rawlings. 6.30 p.m., dinner at the Royal Hotel, followed by an informal quiz session. The local secretary is Dr. Ross Webster, Lister House, Horsham.

Swan Hill.—On Saturday, October 14, the following course will be given: 2 p.m., "Treatment with Steroids", Professor R. R. H. Lovell; 3.15 p.m., "Head Injuries", Mr. J. K. Henderson; 4.45 p.m., "Resuscitation of the Newborn", Dr. W. A. Kitchen. The local secretary is Dr. Hugh Melville, 22 Beveridge Street, Swan Hill.

Wangaratta.—On Saturday, October 21, in the Blood Bank Waiting Room, at Wangaratta Base Hospital, the following course will commence at 2.30 p.m.: "Cardiac Arrhythmia", Dr. M. J. Etheridge; "Depressive States", Dr. J. F. J. Cade; "Clinical Disorders of Thyroid Gland", Dr. Kenneth Fairley. The local secretary is Dr. Matthew Rohan, 18 Docker Street, Wangaratta.

Post-Graduate Facilities at the Royal Women's Hospital.

Facilities now exist at this hospital for residence for post-graduates desirous of attending the hospital for post-graduate study. At any one time, it will be possible to offer residence to four post-graduates. The Post-Graduate Subcommittee of the hospital has designed methods of offering opportunities to general practitioners who desire the opportunity to observe the work carried out in an obstetrical and gynæcological teaching hospital. There is no fee for teaching, but the hospital's Board of Management charge £7 per week for the residence. Further information is available from the Medical Superintendent, Royal Women's Hospital, 720 Swanston Street, Melbourne. Telephone: FJ 9441.

Recorded Lectures.

The following recorded lectures have been added to the Committee's library of ten-inch microgroove discs, and may be borrowed on request without fee: "Hyponatræmia (The Sea Within Us)", by Dr. George A. Perera, of New York—2 discs; "Diagnostic and Prognostic Evaluation of the Hypertensive Patient", by Dr. Perera—2 discs.

Address.

The address of the Melbourne Medical Post-Graduate Committee is 394 Albert Street, East Melbourne, Victoria. Telephone: FB 2547.

Deaths.

THE following death has been announced:

TOWNLEY.—Kenneth Russell Townley, on August 31, 1961, at Brisbane, Queensland.

Diary for the Month.

SEPTEMBER 18.—Victorian Branch, B.M.A.: Finance Sub-Committee.
SEPTEMBER 19.—New South Wales Branch, B.M.A.: Medical Politics Committee.
SEPTEMBER 20.—Western Australian Branch, B.M.A.: General Meeting.
SEPTEMBER 20.—Victorian Branch, B.M.A.: Clinical Meeting (Victorian Eye and Ear Hospital).
SEPTEMBER 21.—Victorian Branch, B.M.A.: Executive Meeting of Branch Council.
SEPTEMBER 21.—New South Wales Branch, B.M.A.: Clinical Meeting.
SEPTEMBER 22.—Queensland Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): Medical Officers to Sydney City Council. All contract practice appointments in New South Wales. Members are requested to consult the Medical Secretary before undertaking practice in dwellings owned by the Housing Commission.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

Authors of papers are asked to state for inclusion in the title their principal qualifications as well as their relevant appointment and/or the unit, hospital or department from which the paper comes.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full data in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: 68-2651-2-3.)

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